SCIENCE

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AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

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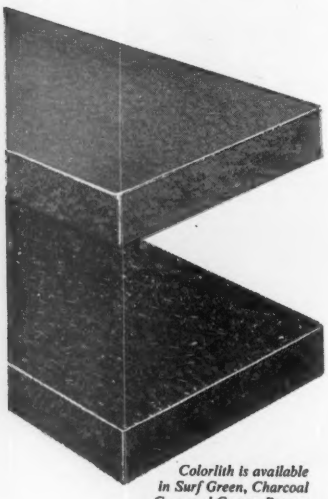

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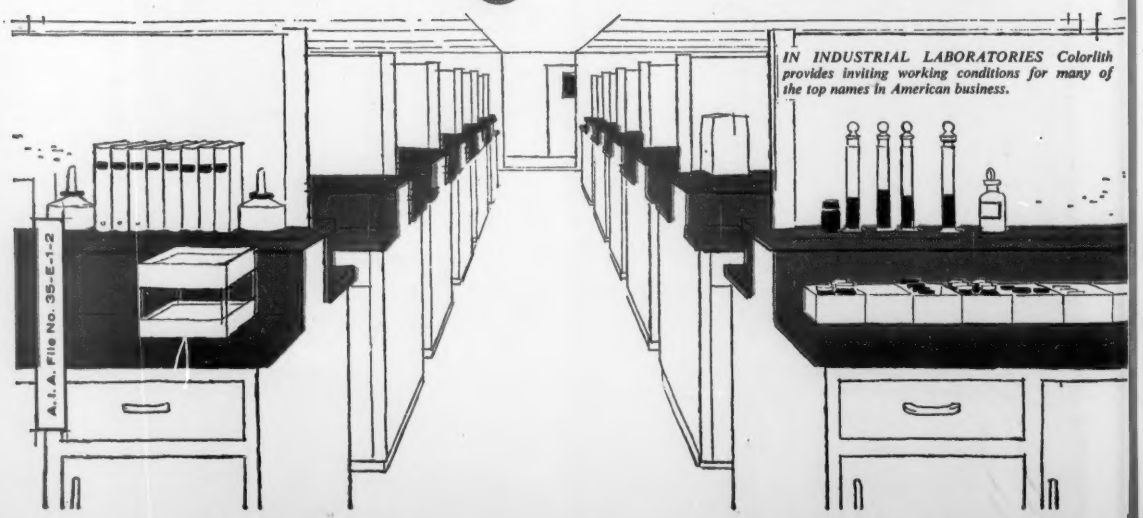

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Francis Bacon...on studies

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—*Essays 50. Of Studies, 1625.*

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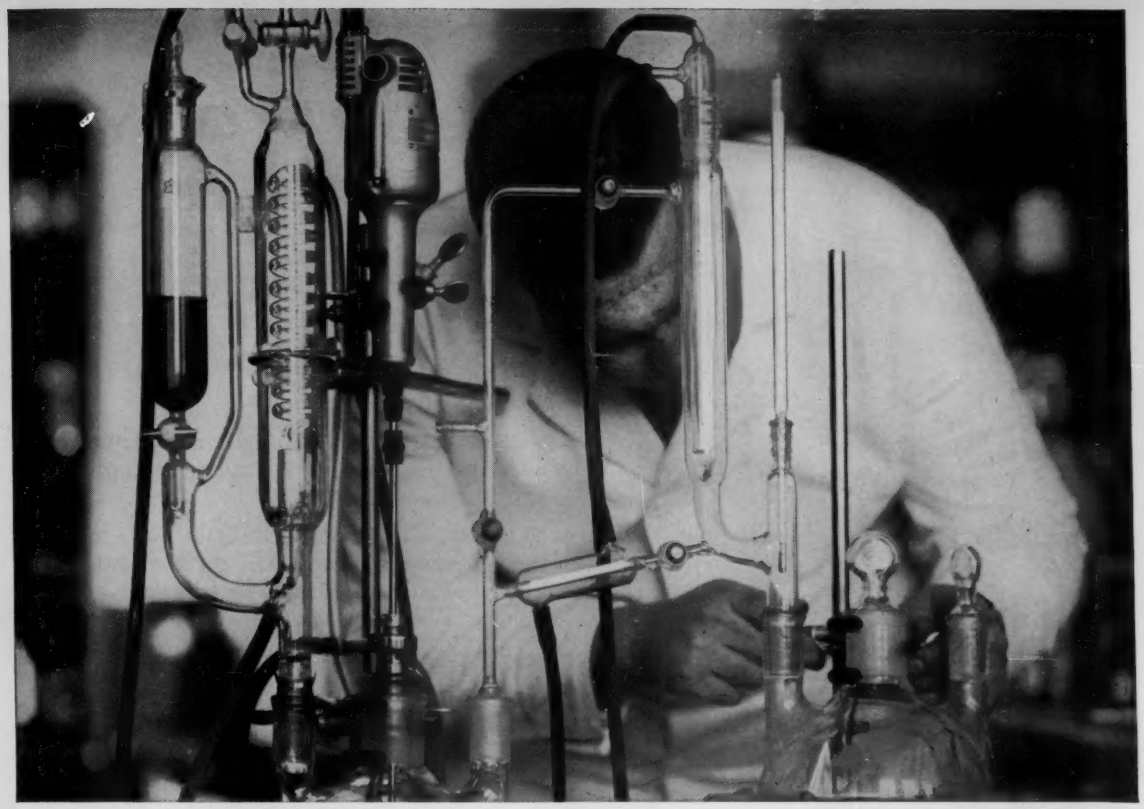

How organic chemists put lithium to work

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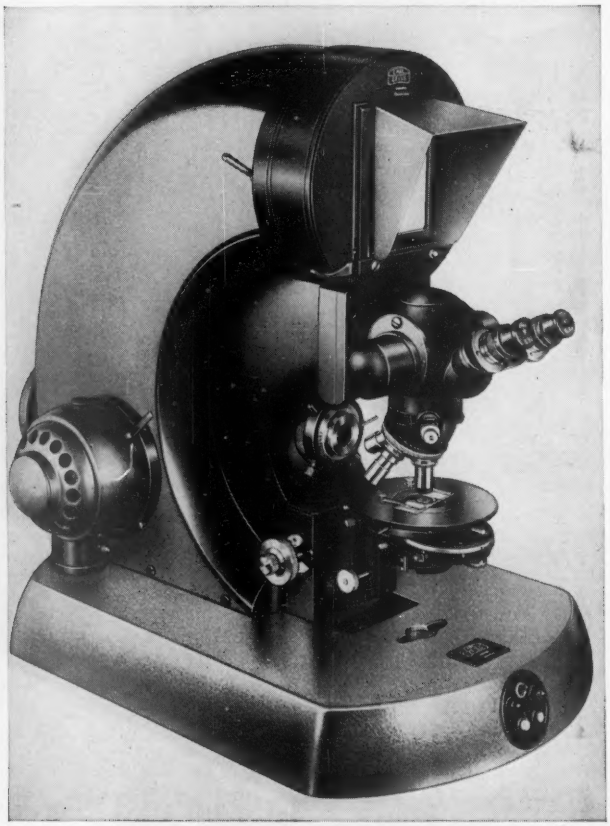

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a run of luck in the optical design department . . . a continuous reactor on an academic scale . . . how to get started right, or even wrong

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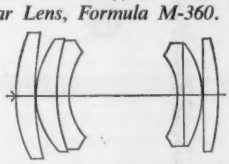
After all these years—the recent ones with high-speed digital computers helping—it surprises outsiders that lens designers should still expect to find new combinations of curvatures, refractive indices, thicknesses, and spacings that will substantially improve photographic lens performance. But they do, to the pain of the authors of yesteryear's superlatives. A sort of continuous auction goes on, at which optical manufacturers keep bidding up the number of lines per millimeter resolved on film in accordance with Method 7 of MIL-STD-150.

chemist as chemical engineer

In 6-inch to 12-inch focal lengths for 70mm aerial film at relative apertures around *f*/2.8 to *f*/3.5, we revel for the moment in beating the previous high by nearly twice. We have had a run of good luck in recent months. We did it with our 6-inch *f*/2.8 *Kodak Aero Ektar Lens, Formula M-360*. Here



are the minimum resolution figures we get at full aperture for a sample lens of this formula photographing high-contrast, 3-line, clear-on-black resolution targets on Kodak Super-XX Aerial Recon Film with white light through a Kodak Wratten No. 12 Filter:

semi-field	8°	2.5°	5°	7.5°	10°	12.5°	15°
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These figures are very close to what used to be quoted for the capabilities of the film itself. Only nowadays our film people smile at the conceptual *naiveté* of a resolving power figure for film. Only the resolving power of the film-lens combination retains some significance. This significance, too, tends to attenuate after an hour at the blackboard with an earnest man.

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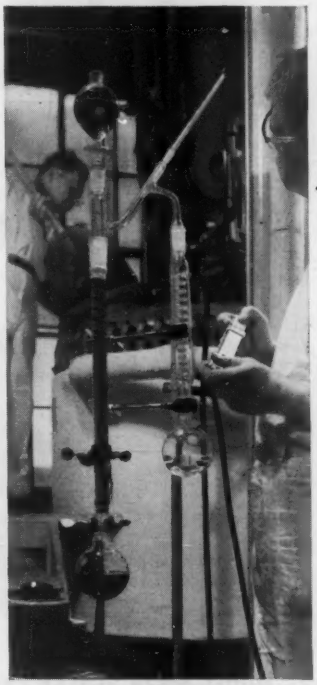

chemical engineer as chemist

Many organic compounds are manufactured in quantity by shoveling in the reactants and cooking. The "batch method" scales the 1-liter flask up to the 200-gallon kettle. We have gone the other way. We assemble common laboratory ware on a table top and operate it like a packed tower in a chemical plant. The nearer chap is running the reaction

$$C_6H_5CHO + H_2C(COOC_2H_5)_2 \rightleftharpoons C_6H_5CH{=}C(COOC_2H_5)_2 + H_2O.$$

He turns up his voltage regulator to keep the column just hot enough for the water to distill off. This keeps the reaction going. As long as the reactants, with a little piperidinium benzoate as catalyst are supplied to the funnel, his product collects in the bottom flask. Ethyl benzalmalonate is made all day long, yet the materials are subjected to reaction conditions for only 30 seconds. Very little time for decomposition and side reactions. For a 0.7 mole run he gets in 30 minutes as much product and yield—at better quality—as in 18 hours by batch technique. Some reactions otherwise quite impractical in the academic laboratory, e.g. chlorination of xylene, run slick as glass.

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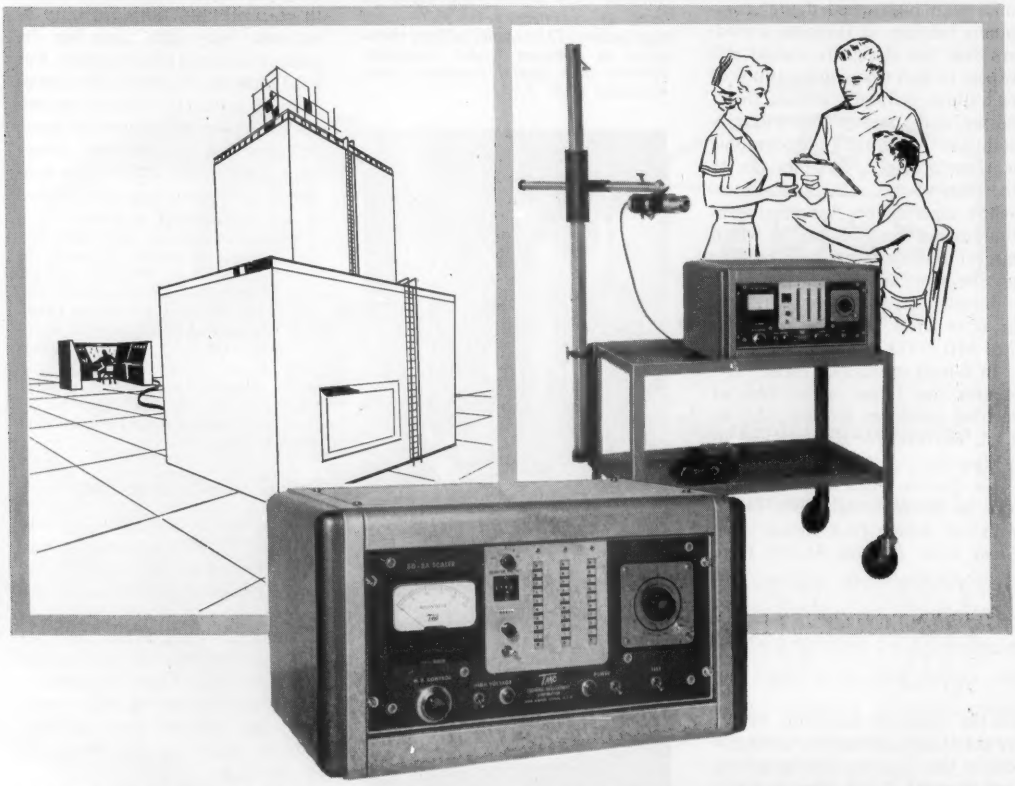

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SCIENCE

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The question of what to do with research equipment after the program has been completed is a special source of difficulty under the contract arrangement. The equipment to be disposed of may range from portable things like glassware to permanent installations like nuclear reactors or linear accelerators. The procedure by which the Government divests itself of ownership of either portable or fixed equipment under contract arrangements is cumbersome and expensive. Portable equipment may be sent to a warehouse while lists describing it are circulated throughout the Government. If no federal agency wants the equipment, it may be declared surplus and put up for sale. The handling and accounting often costs more than the material is worth. Even for permanent installations, the problem is complicated by legal requirements. Generally the Government works out arrangements whereby the research institution may acquire ownership, but here again much paperwork and expense is entailed. Under grants, on the contrary, the granting agency may choose to make all equipment purchased for the project the property of the recipient institution from the outset.

Companion bills that extend the right to make grants to those agencies now limited to making contracts for basic research are now in committees of the House and the Senate. All of the agencies, both those that now make grants and those that do not, favor the bills, and there is apparently no opposition to their passage in Congress. On the contrary, it appears that there is general agreement that the bills would benefit universities, improve relations between the agencies and the universities, and simplify the administration of research—and all of this at no increase in costs.

Despite this agreement, these bills may be tossed aside during the rush toward adjournment unless they get some public support. This is especially likely to happen to the bill in the House, which is entitled "H.R. 13091, a bill to authorize the expenditure of funds through grants for the support of scientific research and other purposes." Those who favor the bill should express their support by writing to Representative Oren Harris, who introduced it in the House and who is chairman of the Committee on Interstate and Foreign Commerce, to which it was referred. For a greater effect, a copy of this letter should also be sent to district representatives. Such support might tip the balance in favor of a good, sensible, but not very exciting piece of legislation.—G.DuS.

11 July 1958, Volume 128, Number 3315 SCIENCE

Human Vigilance

The rate of observing an instrument is controlled by the schedule of signal detections.

James G. Holland

Current interest in the classical problem of sustained efficiency in monotonous perceptual tasks has centered around situations in which human beings are required to monitor some display in search of critical, but infrequent, signals. Such tasks are numerous and of considerable practical importance. In air defense systems, operators must search radarscopes for extremely infrequent enemy targets. Increased automation requires human monitoring of equipment which seldom fails. In addition, cases involving assembly-line inspection of products represent another large group of monitoring tasks in which the critical signals may arise relatively infrequently.

Recent work on operators monitoring displays having infrequent signals indicates a drop in the percentage of signals detected as time on watch progresses. Mackworth (*1*) has shown a decrement in the subject's ability to detect signals as a two-hour watch progressed. The signals were double steps of a clock hand which normally stepped 0.3 inches every second but had 24 double steps per hour. Similar decrements have been demonstrated (*2–6*) when subjects were required to detect targets on simulated radar displays. Field studies also have shown the decrement as time on watch passes. This has been found true for radar operators (*6, 7*) and for a variety of industrial inspectors (*8*). In addition, Bakan (*9*), using a modified threshold measurement technique, has demonstrated a decrement in a brightness discrimination task.

Not all investigators have found a decrement. One investigator (*10*), using the clock test, has shown an increased variance in the number of detections as the watch progresses, but no average decrement. Others (*4, 11*), using latency of detection of nontransient signals as a criterion, rather than the percentage of signals detected, have found an increase in variance but no increase in the average latency of detection.

Whether a decrement is found or not, the fact is clear that many signals well above absolute threshold are not detected either early or late in the session. Furthermore, if the frequency of signals increases, there is an increase in the percentage of signals detected (*4, 5*). For example, Deese found that with a display simulating a search-radar 'scope and using 10, 20, 30, or 40 targets per hour during a three-hour watch, 46, 64, 83, and 88 percent were detected, respectively.

In order to "account for" the decrement and the relation between signal frequency and detection probability, an abundance of theoretical constructs have been offered. The results obtained are said to reflect declines in, or waxing and waning of, attention, vigilance, or fatigue. Mackworth (*1*) tentatively postulated an excitatory state termed "vigilance" which is opposed by an inhibitory state that parallels the concept of external inhibition found in the literature on classical conditioning. More recently, Adams (*2*) has used Hull's I_R (reactive inhibition) in a similar manner. The performance decrement is supposed to be a partial extinction phenomenon reflecting the build-up of the inhibitory state. When a verbal message to the effect that the subject should "do even better for the rest of the test" was delivered, the percentage of signals detected returned to the initial level. This is explained as disinhibition and thus as evidence for the existence of an inhibitory state. When a 1-hour break was provided, again the performance returned to the initial level. This is said to reflect spontaneous recovery from the inhibitory state.

Several investigators have employed expectancy as an explanatory concept. Mackworth (*6*), Broadbent (*11*), and Deese (*12*) have used it to "explain" (i) the greater over-all percentage of detections when the number of signals per session increases (*4, 5*), and (ii) the increased probability of detection for the longer intersignal times that is observed when a signal-by-signal analysis is made (*1, 5*). [The latter finding has not always been confirmed (*3, 5*).] In addition, Broadbent has used the idea of stimulus selectivity (that is, attention or set) to explain not only the findings concerning monitoring behavior but classical conditioning as well.

In addition to these theories relative to psychic and conceptual states, a physiological theory has been advanced. Deese suggested that the waking center (*12*) of the hypothalamus may be involved and that the activity of the center depends on an influx of sensory stimulation. According to this theory, as it applies to problems of detecting infrequent signals, a varied sensory input is necessary to maintain the excitatory state in this center and thus to maintain a high level of detection.

Need for an Atheoretic Approach

The various theories have all been developed to account for a rather meager set of data. The parameters influencing

The author is a member of the staff of the Psychological Laboratories, Harvard University, Cambridge, Mass.

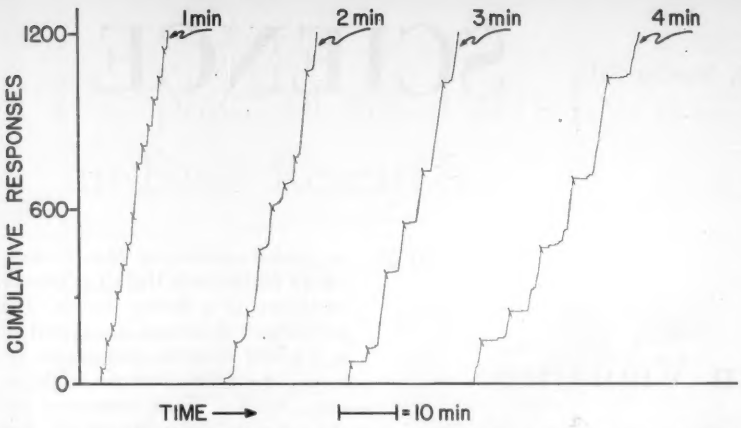

Fig. 1. Cumulative response records for 1-, 2-, 3-, and 4-minute fixed-interval schedules of pointer deflections. Detections are indicated by lines cutting across the records.

the monitoring of low-signal-frequency displays are as yet poorly explored, with the result that inconsistencies are found among the findings. In view of this state of affairs it might be well to forego the luxury of developing explanatory concepts until the empirical relations are better established.

Indeed, the necessity for theories has been sensibly challenged by Skinner (*13*) with regard to theories of learning. Theories, in Skinner's sense, are explanations of data that make use of events at another level of observation and are not to be equated with empirically defined concepts which refer to the behavioral level of observation. The latter permit generalization of empirical principles. His arguments seem at least as relevant to theories of "vigilance."

Such entities as vigilance, attention, inhibition, expectancy, and waking-center activity all fall into the category of theories, as defined above. They, like concepts in learning theories, are "at some other level of observation, described in different terms, and measured, if at all, in different dimensions" (*13*, p. 193). These concepts give the appearance of explaining the data because of the syntax of the statements. The subject is said to make a detection because he is, at that moment, vigilant or attentive or expecting a signal. But the concepts are no less mysterious than the phenomena they purport to explain. There remains the task of discovering the events which influence vigilance, attention, or expectancy. Once having done this, we may be little better off than if we had simply searched for the conditions controlling the probability of detection, since this is assumed to be directly related to the intervening explanatory concept.

The argument that theories generate research does not seem to apply to theories in this area. With one exception (*5*), the theories seem to have been offered as explanations of data already collected. But even should they generate research in the future, it is by no means obvious that this research would be of greater significance than research directed toward an empirical and behavioral systematization of the field.

However, the use of theories is by no means surprising in view of the types of measure used. In practice, only the percentage of signals detected, latency of detection, or change in threshold intensity is measured. The investigator is then faced with the problem of saying what it is that changes during the monitoring task. It is unsatisfactory to say that the percentage of signals detected *is* the vigilance rather than a *result* of vigilance, attention, or expectancy, just as the learning theorist is unsatisfied in saying that decrease in errors *is* learning. Instead of proceeding to search for a satisfactory datum on the behavioral level of observation, the investigator postulates events for other levels of observation. Signal detection is said to *reflect* states of vigilance, attention, or expectancy. The result of this is that the search for an appropriate behavioral datum is impeded, and in its place assumed causes are used which are mental, physiological, or conceptual events not describable in behavioral terms.

One approach to discovering a satisfactory datum is to consider the behavior which may be involved in monitoring and then to determine the variables which control that behavior. Success in detecting signals may depend on the emission of responses which will make the detection possible. These could be responses of orienting toward the correct portion of the display and fixating or scanning the display. Such responses can be termed observing responses in that they bring about the observation of signals (*14*). Furthermore, these observing responses might follow the same principles as instrumental responses and thus be subject to control by the same type of environmental variables. It is suggested that the observing responses which make detections possible follow the principles of operant behavior. The reinforcement for these observing responses could be the detection of the signals. That is to say, the detection itself could exert control over the rate or probability of emission of observing responses in exactly the same manner as food reinforcement controls the rate of operant responses in animals.

Signal Detection as Reinforcement

In order to evaluate this formulation of "vigilance" it was first necessary to determine whether signal detection really could serve to reinforce an observing response. To do this, subjects (Navy enlisted men), working in the dark, were required to report deflections of a pointer on a dial; but the pointer could be seen only when the subject pressed a key which provided a brief flash of light that illuminated the face of the dial. When the key was pressed, the light flashed for a period of only 0.07 second, even if the subject held the key down. Thus he had to release and redepress the key to obtain another look at the dial. When the subject observed a pointer deflection he reported it by pressing another key, which reset the pointer. The pointer remained deflected until this key was pressed. The deflections of the pointer were programmed so as to make possible various schedules of detections (or reinforcements). Each subject was advised that his only aim should be to make as many detections as he could and to reset the pointer as rapidly as possible. At the end of each session he was informed of the number of detections made and the average time per detection. He was not informed that the experimenter was in any way concerned with the frequency with which he flashed the light. Cumulative response records were made of his responses on the light-flashing key. This

type of recording, commonly used in operant conditioning (see *15, 16*), consists of a pen which moves in small discrete steps across the recorder paper as responses are made, while the paper moves slowly in a direction perpendicular to the direction of pen movement. The result is a tracing in which the slope of the line reflects the rate of responding.

In order to determine whether signal detection can serve as reinforcement for observing behavior, various schedules of signal presentation were used, analogous to the scheduling of more conventional reinforcers, such as food and water, employed in operant conditioning with animals. Throughout all of the various schedules to be discussed below the subjects were *never* told anything about the nature of the schedule.

Fixed interval. The first schedules used were of the fixed-interval type. Five subjects began with a ½-minute fixed-interval schedule. That is to say, the needle was deflected for ½ minute after each detection and remained deflected until it was reset by the subject. After eight 40-minute sessions, the interval was increased to 1, 2, 3, and finally 4 minutes, with eight successive sessions on each.

Figure 1 presents data from comparable portions of records for a typical subject on several schedules, all of different fixed intervals. Each curve is a segment of record from the last session which the subject had on the indicated fixed interval. The individual curves are displaced along the horizontal axis. The lines cutting across the records indicate signal detections. Shortly after each detection there is a period in which no observing responses are emitted, as indicated by the flat portions of the curves. Then responding (observing) resumes in an accelerated fashion and reaches a high rate before the next signal. These "scallops" are analogous to those obtained with animals working for food reinforcement on a fixed-interval schedule (*15–17*). In either case the data represent a temporal discrimination. Responses immediately after reinforcement are not reinforced, so a discrimination is formed for "no responding following reinforcement." Responding resumes after time passes and the conditions become appropriate for reinforcement.

Examining the records, one could, if so inclined, speculate that they reflect "fluctuations of attention" or the course of "subjective expectancies." However, the temptation to do so should not be great since the dependency of observing rate on detection, or reinforcement, is clear. To postulate states accompanying the changes in observing rate adds nothing of use in controlling or predicting the observing rate.

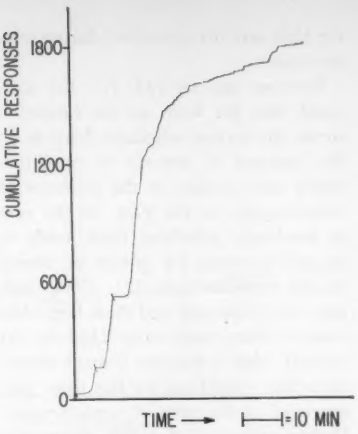

Fig. 2. Cumulative response record showing effect of withholding pointer deflections following a fixed-interval schedule. After three detections (indicated by lines cutting across the record) no further pointer deflections occurred.

Additional insight into the role of signal detection is provided when no further signals occur (that is, during extinction). Extinction data are provided in Fig. 2 for the same subject for whom data were given in Fig. 1. This is a complete record for a 1-hour session. Three signals were first provided on the 4-minute fixed-interval schedule which had maintained the observing behavior for six previous sessions; then no further signals were provided. Following each signal detection in the early portion of the record, the characteristic fixed-interval scallops are found. After the third and final detection there is again a scallop, with the high rate continuing for a time and then gradually declining to a very low value. This decline in rate of observing response is dependent upon the absence of signal detection. It cannot be interpreted as physiological fatigue, since on other schedules higher rates have been maintained, without decrement, for more than three hours.

Fixed ratio. To pursue further the analogy between signal detection and reinforcement as found in typical operant conditioning situations, fixed-ratio schedules were employed. These schedules make reinforcement contingent on the number of responses emitted rather than on the passage of time. To begin with, seven subjects were tested on a fixed-ratio schedule of 36 responses per detection. That is, a needle deflection occurred only after 36 observing responses were made following the immediately preceding detection. After six 40-minute sessions on this schedule the ratio was increased, in blocks of six sessions, to 60, 84, 108, 150, and finally 200 responses per detection. Presented in Fig. 3 is a family of curves for the various ratios for a typical subject. These curves are equivalent segments of the subject's final sessions on the indicated schedules. Tests with these schedules, unlike most monitoring tasks, permit the subject to minimize the number of signals by not re-

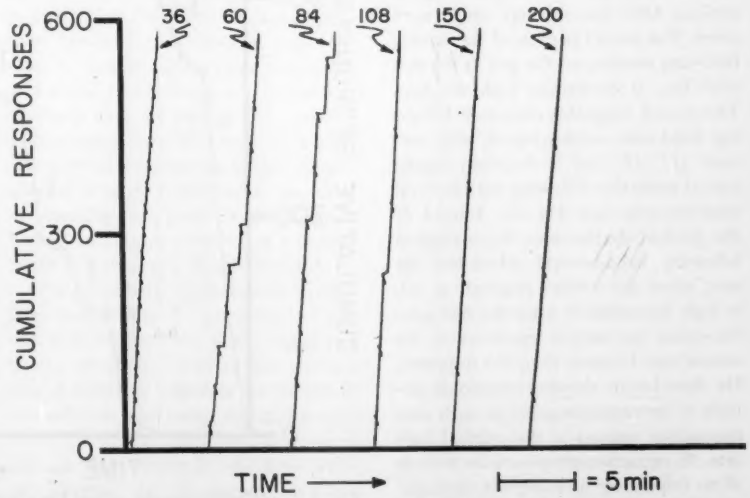

Fig. 3. Cumulative response records for 36-, 60-, 84-, 108-, 150-, and 200-response fixed-ratio schedules of pointer deflections. Detections are indicated by lines cutting across records.

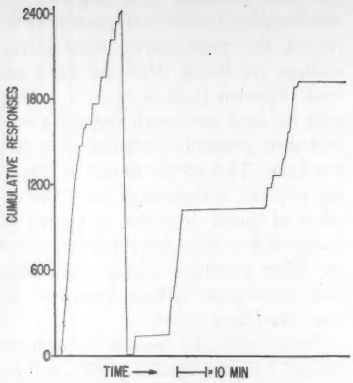

Fig. 4. Cumulative response record showing extinction following a 200-response fixed-interval schedule of pointer deflections. After three detections (indicated by lines cutting across the record) no further pointer deflections occurred.

sponding. Instead, however, he tends to maximize the number of signals by emitting responses at a high rate. Occasionally short breaks or periods of no responding occur, but only immediately following a detection. These results are also characteristic of those obtained with conventional reinforcement on fixed-ratio schedules (*15–17*).

An additional demonstration of the control exerted by the schedule of signal detection or reinforcement is seen in the extinction following fixed-ratio schedules. A 1½-hour extinction record is presented in Fig. 4 for the same subject for whom data were given in Fig. 3. Three needle deflections were provided on the 200-response ratio schedule which he had experienced for the preceding six sessions. After that, no more signals were given. The second portion of the record, following resetting of the pen at the vertical line, is continuous with the first. This record resembles extinction following fixed-ratio reinforcement with animals (*15, 17*) but is decidedly unlike typical extinction following fixed-interval reinforcement (see Fig. 2). Instead of the gradual decline seen for extinction following fixed-interval schedules, the rate, when the subject responds at all, is high. Immediately after the last reinforcement the subject continues at his normal rate for more than 800 responses. He then begins showing occasional periods of no responding, but in each case responding resumes at the original high rate. As extinction progresses the periods of no responding increase, but, throughout the session, when there is a single response there is a run of responding at the high rate that prevailed during reinforcement.

Previous analysis (*13, 17*) has indicated that the form of the extinction curves for various schedules depends on the presence or absence of conditions which were present at the moments of reinforcement in the past. In the case of fixed-ratio schedules there tends to be reinforcement for groups of closely spaced responses (see *15*). Thus, high rates are reinforced, and these high rates come to characterize ratio schedules. As a result, when a response is made during extinction, conditions are like those that prevailed at the time of reinforcement. During extinction, therefore, intermediate rates are lacking. The subject either responds rapidly or not at all.

Multiple schedule. It has also proved possible in operant conditioning to generate behavior appropriate to more than one schedule in a single organism during the same session (*17*). To do so, stimuli are provided to indicate which schedule is in effect at a given moment. The stimuli used have been alternation of schedules (called mixed schedules), different colored stimulus lights, or both. I have successfully combined a 40-response fixed-ratio and a 3-minute fixed-interval schedule, using four subjects. These tests began with six 40-minute sessions in which a small red light indicated a fixed ratio of 23 responses to be in effect and a small green light indicated a ½-minute fixed interval to be in effect. The order of appearance for these two schedules was randomly determined. Then for sessions 6 through 11, the schedules were changed to a 40-response fixed ratio and a 3-minute fixed interval. These two schedules were alternated regularly. Then for the twelfth and final 40-minute session the two schedules appeared randomly, with only the stimulus light providing the basis for discrimination. A typical record for this session is presented in Fig. 5. The 3-minute fixed-interval portions of the record are labeled *I*, and the 40-response fixed-ratio portions are labeled *R*. It can be seen that when the interval was in effect (green light on) the subject's observing rate provided the fixed-interval scallop. (There is a rougher grain to the scallop than to that found in Fig. 1. This is probably due to the experience on fixed-ratio schedules.) When the fixed-ratio schedule was in effect (red light on), the subject's observing rate was that typical for fixed-ratio reinforcement. Thus, like other operant behavior, the observing response can be brought under stimulus control. There remains no need to appeal to another level of analysis by speaking of "attention" being dependent on "context" or "meaning." Such proposed constructs are unnecessary when the control exerted by the schedule of detection under correlated stimuli can be directly demonstrated.

Differential reinforcement of low rates. One further schedule which attests to the control of observing rate by detections is one which makes detections (reinforce-

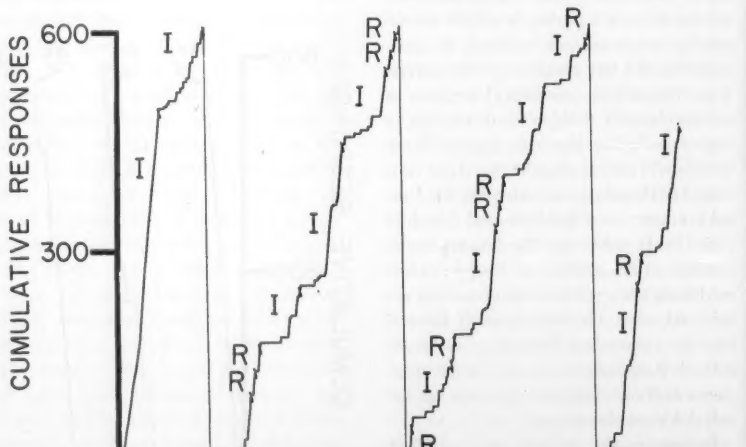

Fig. 5. Cumulative response record for a multiple schedule consisting of a 3-minute fixed interval (*I*) and a 40-response fixed ratio (*R*). Lines cutting across the record indicate detections.

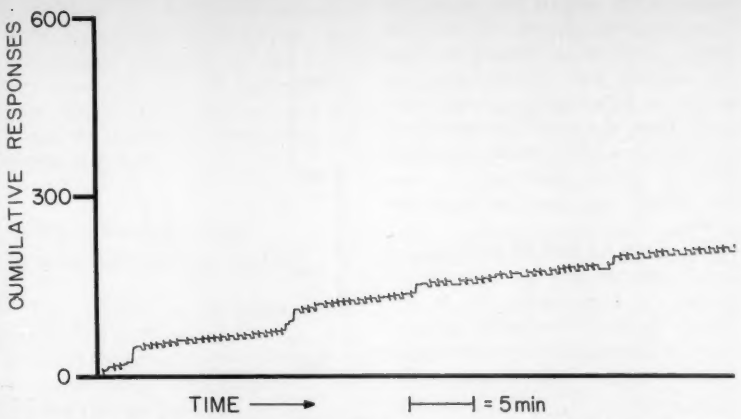

Fig. 6. Cumulative response record for differential reinforcement of a low rate. Downward deflection of the pen indicates pointer deflection, and upward deflection indicates detection. Pointer deflections occurred only after no observing response was emitted for 30 seconds.

ments) contingent on low rates of responding. Two subjects were placed on such a schedule. The needle was deflected only after they had failed to emit an observing response for 30 seconds. A record of one subject's fourth 1-hour session is presented in Fig. 6. It can be seen that this schedule provides a very low rate of responding, like that found in other operant conditioning experiments (*18, 19*) for which similar schedules were used. The few short bursts of higher rates tend to occur after the subject responded just a little sooner than the required 30 seconds. Even this detail parallels results with animals working for food on this schedule (*18*).

Conclusion. The results reported thus far demonstrate that signal detections can control the rate or probability of emission of observing responses. Furthermore, this control is of the same nature as that exerted by conventional reinforcers, thereby permitting the conclusion that signal detections serve as reinforcements for observing responses.

Observing Rates and "Vigilance"

There remains the problem of determining whether the schedules used in classical vigilance studies will generate observing rates which parallel the probability-of-detection data found in those studies. A decrement in probability of detection during the course of a session has been shown (*5*) for 20 signals per hour when the signals were arranged randomly through the session with the intersignal times drawn from a rectangular distribution. Such a schedule, in operant conditioning terms, would be a variable-interval schedule having an average interval of 3 minutes. Four subjects were placed on this schedule. Figure 7 shows the records for two of these subjects during their first session. (Vigilance studies frequently have only one session.) These records were chosen by way of illustration because these two subjects were the two extremes in terms of decrement of response rate as the session progressed. All four subjects showed periods of lower observing rates in the latter portions of the session. The drop in rate as the session progresses is brought about by the fact that reinforcement frequency is insufficient to maintain the higher initial rate, which results in part from the subject's past experience. However, some decline does continue to appear within each session for as many as 18 additional 1-hour sessions. Similarly data on pigeons (*17*) show a within-session decline in rate on a variable-interval schedule when the average interval is long. Furthermore, the drop in observing rate parallels the frequent finding, in viligance studies, of a decline in the percentage of signals detected.

It has also been demonstrated in vigilance studies that the percentage of signals detected increases as the signal frequency increases. To determine whether rate of observing responses also increases, two subjects were tested on various variable-interval schedules; first there were three 1-hour sessions in which the average interval was 15 seconds (240 per hour), then the interval was increased, in blocks of three sessions, to 30 seconds (120 per hour), 1 minute (60 per hour), and finally 2 minutes (30 per hour). In each case the distribution of intervals was rectangular, varying from 5 seconds to double the average interval. In Figure 8 there is shown a family of curves for one subject for these various average intervals. These records are for the first 3000 responses of the final session on each schedule. It can clearly be seen that the rate of observing is highest for the high signal rate and decreases as the signal rate decreases. Again this finding parallels the results of classical vigilance studies in the higher percentage of detection for higher signal rates (*5*), and at the same time it parallels other operant conditioning research with variable-interval reinforcement which also shows high response rates to be associated with schedules having a low average interval (*15, 17*).

The curvature seen in the records in Fig. 8 is also of some interest. For the average interval of 2 minutes there is a decline in observing rate as the interval progresses, while for the 15- and 30-second average intervals there is an increase in observing rate. The decrease shown in the case where the smallest number of signals is used is another illustration of a decrement in "vigilance." When larger numbers of signals are used, the "vigilance" literature reports and the present study shows that the decline during the session disappears. Actually, most studies are incapable of showing a rise in probability of detection because the signal is set so that initial detection is nearly always made.

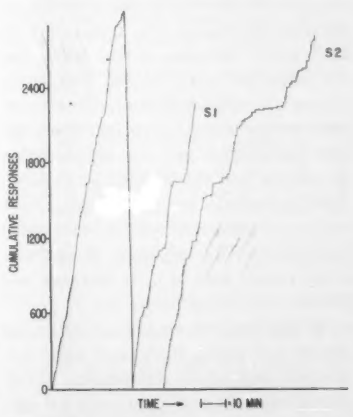

Fig. 7. Cumulative response records for the first session for two subjects (*S1* and *S2*) on a variable-interval schedule with average interval of 3 minutes (rectangular distribution ranging from 5 seconds to 6 minutes).

Observing Behavior with the Mackworth Schedule

Additional evidence for the adequacy of the observing-behavior analysis of "vigilance" is seen when the schedule used by Macworth (*1*) is employed in the present study. The aims of this study were (i) to determine whether the schedule of signals actually used by Mackworth would confirm the data on decrement in percentage of detections found by him and at the same time provide data on decrement in observing rate, and (ii) to determine whether the data on observing rate would parallel the data on percentage of signals detected. In all of the experiments reported above, signals which remained until detected (nontransient signals) were used in order that the schedule of detections would be under the experimenter's control. The result was that signals could never be missed. But in order to determine whether the typical vigilance measure of percentage of signals detected is paralleled by the observing rate, it was necessary to make the signal automatically disappear if it was not detected within a short time (these are called transient signals). The general procedure was identical with that previously used except for the fact that when the needle was deflected it returned to its original position after 1¼ seconds unless the subject previously detected and reset in in the usual fashion by pressing the key which indicated a detection. The schedule of pointer deflections was identical with the schedule of double jumps used by Mackworth (*1*) in his clock tests, which stand as the classics in the area of vigilance. This sequence of intervals between needle deflections was ¾, ¾, 1½, 2, 2, 1, 5, 1, 1, 2, 3, and 10 minutes, in that order, and the sequence was repeated four times during the 2-hour sessions. Thus there were twelve signals each half-hour, the shortest interval between signals being ¾ minute and the longest, 10 minutes. Sixteen subjects served in two 2-hour sessions. Cumulative records were made of their observing responses. In addition, a record was kept of their successes and failures in making detections.

In Mackworth's studies, as well as in the present study, there were some important individual differences. Mackworth found that 29 percent of his subjects missed not more than one signal in the last three half-hour periods. In the present study 39 percent of the subjects missed not more than one signal in the entire two hours. The vigilance decrement is thus due to the performance of the other subjects. It turns out that the high-detection subjects show rather different observing response rates than the others. Therefore, in treating the data the subjects were divided into two groups—a high-detection group, made up of those who missed not more than one signal in a 2-hour session, and a low-detection group, made up of those who missed more than one signal per session.

The results for both the percentage of signals detected and for observing responses are summarized in Fig. 9. The data for the two 2-hour sessions are combined and show the means for each half-hour period for both measures. The curve labeled *D–H* (open circles) represents the percentage-detection data for the high-vigilance group. It shows, of course, nearly perfect detection throughout, since this was the basis for assignment to this group. The curve labeled *R–H* (open triangles) shows the mean number of observing responses for this high-vigilance group. Interestingly, these subjects actually show a rise in response rate as the session progressed. Their percentage-detection data cannot reflect this rise because these subjects are already detecting nearly all the signals. It is probable that this group has an increased detection efficiency which cannot be revealed by the detection measure. Classical vigilance studies have had no measure of observing rate and therefore have been unable to show such a phenomenon.

The low-vigilance group's detection results are shown in the curve labeled *D–L* (solid circles) and their observing response results, in the curve labeled *R–L* (solid triangles). By the second half-hour there is a drop both in the percentage of signals detected and in the rate of observing responses. In the first half-hour members of this group detected 93 percent of the signals and emitted an average of approximately 5100 observing responses, while in the second half-hour they detected 74 percent of the signals and emitted an average of about 4550 observing responses. The drop from the first to the second half-hour is significant at the 1 percent level for both measures. The slight decline from the second to the third half-hour is not significant for either measure. But the rise in the fourth half-hour is significant at the 5 percent level for both measures. This end-spurt is probably due to the fact that the subjects knew that the session was 2 hours long. Mackworth found no such end-spurt, but other studies (*5*) have shown that knowledge

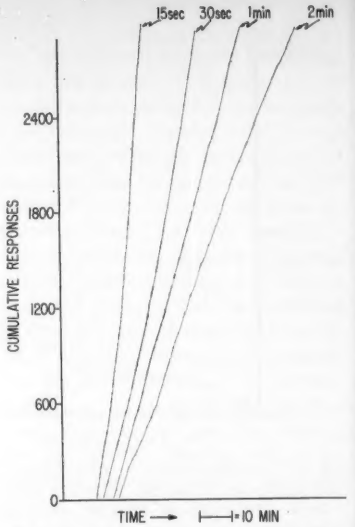

Fig. 8. Cumulative response records for variable-interval schedules with average intervals of 15 seconds, 30 seconds, 1 minute, and 2 minutes, respectively (rectangular distributions ranging from 5 seconds to double the average interval). All records are from the same subject. In each case the record was made after three previous sessions on the schedule.

of the length of the session can produce such an effect.

In general, then, the vigilance decrement found by Mackworth was confirmed in this study, and a parallel decrement in observing rate was shown as well. It should be recalled that detections (that is, reinforcements) on variable-interval schedules show that the lower the rate of signals, the lower the rate of responding (see Fig. 8). Thus, when signals are missed, this might have the effect of lowering the rate, since the subject is then on a different variable-interval schedule with a higher average interval.

One further factor may have an influence on the response rate in this study. When transient signals are used, the situation is analogous to work with animals in which a variable-interval schedule is used, with the added contingency that when the program is set up for reinforcement, the animals have only a brief time in which to respond before reinforcement is no longer available. Such a schedule (*17*) used with animals (called "variable interval with limited hold") has shown that the use of a limited hold considerably increases the rate of response over that for the same variable-interval schedule with unlimited hold. This presumably results from the differential reinforcement of high rates, since high rates of responding are more likely

to be reinforced in the case of limited hold. There may well be an analogous effect in this study. Those subjects who detect almost all signals are very probably being reinforced for high response rates, with the result that their rate increases and thus maintains maximum detection proficiency.

Additional Parallels between Response Rate and Detection Data

The similarity in the shapes of the curves in Fig. 9 for the observing rate data and the detection data for the low-detection group offers support to the position that the finding of classical vigilance studies could reflect observing behavior. Additional evidence may be adduced for this in parallels between vigilance data and work on operant behavior from animal laboratories. For example, (i) Mackworth (*6*) finds that giving subjects 10 milligrams of benzedrine raises the level of detection. Similarly Brady (*20*) has shown that doses of benzedrine administered to rats provide high response rates when the rats are on a variable-interval schedule. (ii) In addition, Mackworth (*6*) has shown that high room temperatures result in lower levels of detection; and, similarly, animals on a variable-interval schedule show lower response rates when the room temperature is high (*21*). (iii) Nicely and Miller (*22*) have investigated the effect of unequal spatial distribution of signals on a radar display. The strobe line rotated at 6 revolutions per minute. One quadrant had signals on an average of one every five rotations, while the remainder of the display had signals on an average of one every 30 rotations. Nicely and Miller found that the percentage of signals detected increased for the high signal-frequency area and declined for the low signal-frequency area. After 30 minutes the detection-data curve for the high signal-frequency area had approached a higher asymptote than had that for the low signal-frequency area. This situation is analogous to a multiple schedule having a 40-second average variable-interval schedule with one stimulus (one area) and a 5-minute average variable interval with another stimulus (the other area). Ferster and Skinner (*17*) have shown that animals on such a multiple schedule show a lower response rate in the presence of the stimulus correlated with the long variable interval than in the presence of the stimulus correlated with the short variable interval. (iv) It has been demonstrated that rest periods restore the detection efficiency to nearly what it was at the beginning of the session (*1, 2*). Similarly, Ferster and Skinner (*17*) have found that response rates on variable-interval schedules are increased by interspersing rest periods.

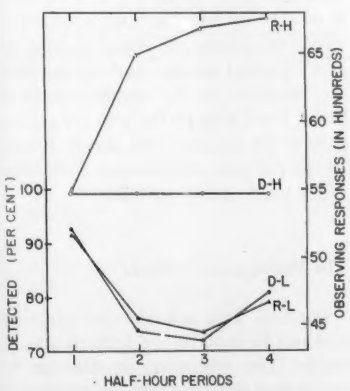

Fig. 9. Mean percentage of signals detected and mean number of observing responses per half-hour period for a two-hour session on the Mackworth schedule. Curve *R-H*, observing response data for the high-detection group; curve *D-H*, detection data for the high-vigilance group; curve *R-L*, observing response data for the low-detection group; curve *D-L*, detection data for the low-detection group.

Conclusions and Implications

This analysis (*23*) has demonstrated that detections of signals can serve as reinforcements for observing responses and, further, that the detection data of vigilance studies may reflect the observing response rates generated by the particular schedules employed. Thus a means of analysis is provided which does not appeal to a nonbehavioral level.

In other vigilance studies the observing behavior has probably been fixation and scanning with the head and eyes as well as perhaps more subtle responses. It would be of interest to extend the present technique to some of these responses, although for many problems the topography of the response may be unimportant and the present methods entirely sufficient.

So far as application is concerned, the striking fact is the rather precise control exerted by the environment over the human operator's observing behavior. Thus, in a man-machine system it should be possible for the machine to maintain control over the operator's monitoring behavior. The ideal manner for exerting such control remains to be worked out. It is hoped that this will be the goal of much additional research in this area. But one obvious way is to provide a high rate of realistic artificial signals on a schedule which would provide the desired observing rate. The most promising schedule for many situations would be a variable-interval schedule of signals having a short duration, like the limited hold in animal work. Other do's and don'ts of the engineering of monitoring tasks must be worked out. To this end it is clear that the abundant amount of systematic research on operant behavior that has been done with animals should be a fruitful source of ideas for developmental research as well as for educated guesses in designing man-machine systems requiring monitoring by human beings.

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Photosynthesis

Experiments at the Max Planck Institute for Cell Physiology, Berlin-Dahlem, 1950–57, are described.

Otto Warburg

Ever since *Chlorella* has been an object of photosynthetic study, it has been known that there are cells that use light efficiently and cells that use light inefficiently. In recent years we have sought to discover and control the conditions that give rise to efficient cells. It has been found that one of the most important conditions is the light intensity at which the cells are cultured. If one employs artificial light sources without interruption, as has been the almost universal practice, the *Chlorella* are then too far removed from their natural living conditions of the past half billion years. The cells are forced to produce organic matter continuously, and more material than they need for their own synthesis. As a consequence, the energy yield of the cells is reduced to a small fraction of the optimum yield.

Cells that use light efficiently result, on the other hand, when one allows the intensity of the light to fluctuate so as to imitate day and night, with dimming late evening and early morning (*1*). We attain this by varying the operating voltage automatically from 50 up to 220 volts and back to 50 volts again over a period of 24 hours. The relative quantum intensities of radiation were measured with the chemical quantum actinometer (*2*), with results indicated by the ordinate values in Fig. 1. Cells so cultured use the light best when they are placed in the manometric vessels in the morning and their photosynthetic efficiency is measured thereafter during the artificial day.

Equally as important as the culturing of the cells are the conditions under which the utilization of the light is measured. For example, it was found with monochromatic light that the utilization of light in the green or yellow or red was the poorer the purer the spectral composition. However, good utilization was immediately restored when a relatively small amount of blue-green light was added to the main beam of very pure monochromatic light. One can thus obtain good or poor yields at will, simply by adding or removing the blue-green light during the measurements of efficiency. If each such test period is made 30 minutes long, one can observe in an experimental day of 8 hours, with one and the same suspension, good yields eight times and poor yields eight times!

The different parts of the blue-green spectrum are not equally effective. The action spectrum of the blue-green light shows a sharp maximum in the region of 460 mμ, as is shown in Fig. 2. This action spectrum is probably a carotinoid spectrum. An inactive carotinoid proenzyme is probably converted by the blue-green light into an active lumino enzyme. As possible analogs, there may be mentioned light-sensitive visual purple, and ooverdin, a carotinoid protein discovered by Richard Kuhn.

Both examples—the fluctuating light during culture and the blue-green light during yield measurement—suffice to make it understandable why, in the last 40 years, in different institutes throughout the world, very different photosynthetic yields have been found—different not in percentages, but in hundreds of percent. Even if the manometry and the light measurements had been correct everywhere, not even approximate agreement would have been possible, owing to ignorance of the essential conditions of culture and measurement. Thus, in the United States, during the years 1938 to 1948, an average quantum requirement of 16 per molecule of oxygen gas produced was found, corresponding to an energy yield of 18 percent in red light. This value is removed from the optimal value (*1*) by several hundred percent.

If one maintains the now-established conditions of good yield, one will obtain good yields from now on, everywhere and always. Figure 3 shows an example of oxygen evolution during constant illumination in a 5-hour experiment in which the quantum requirement per molecule of O_2 produced was approximately 3 for the entire period. Any deviation from linearity with time was within the experimental error. Figure 4 shows oxygen development in a 6-hour experiment in which the quantum requirement per molecule of O_2 produced was approximately 4. Table 1 contains the results of 23 six-hour experiments conducted on 23 days of the months March to May, 1957, in which only a single instance of a poor yield, namely a quantum requirement of 7.5, was obtained (*3*).

The quantum requirement of 3 per molecule of O_2 signifies that in red light about 90 percent of the incident light energy can be converted into chemical energy. Since light energy is freely transformable energy, this energy efficiency is completely compatible with both the first and second laws of thermodynamics. Thermodynamically incompatible with good yields were only those theories concerning the chemical mechanism of photosynthesis that are today at long last recognized as incorrect.

In summary, one can say that, with the fixing of the conditions of culture and measurement, the dispute concerning the efficiency of utilization of sunlight is finally decided. It is a decision in favor of nature. The reaction by which nature transforms the energy of sunlight into chemical energy, and upon which the existence of the organic world is based, is not so imperfect that the greater part of the applied light energy is lost; on the contrary, the reaction is, like the world itself, nearly perfect.

The Multiquanta Problem

But how is it possible that carbonic acid can be split by the light quanta of visible light, which are so deficient in energy that several quanta are necessary? In the photochemistry of the inanimate world, no reactions are known in which several quanta react with *one* molecule at one time, and, moreover, several-quanta reactions are theoretically scarcely conceivable.

The problem was solved several years ago at Dahlem by Dean Burk and us (*4*).

Professor Warburg is director of the Max Planck Institute for Cell Physiology, Berlin-Dahlem, Germany. This article is based on a lecture he delivered in Berlin on 5 Oct. 1957 before the Society of German Chemists. It was first published, in German, in *Angewandte Chemie* [69, 627 (1957)], in collaboration with W. Schröder, G. Krippahl, and H. Klotzsch. This translation was prepared by Dean Burk and George Hobby, National Institutes of Health, U.S. Public Health Service, Bethesda, Md., with the permission of *Angewandte Chemie* and the approval of Professor Warburg.

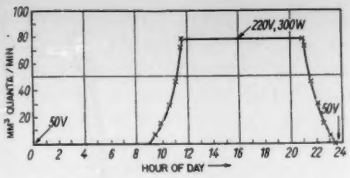

Fig. 1. Fluctuating light intensity in the culturing of *Chlorella*.

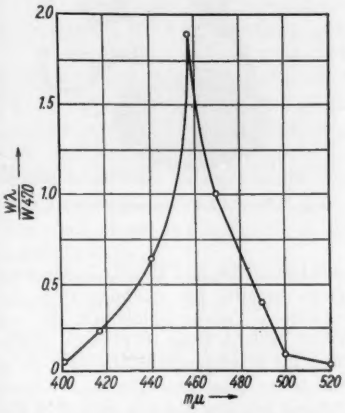

Fig. 2. Action spectrum of blue-green light.

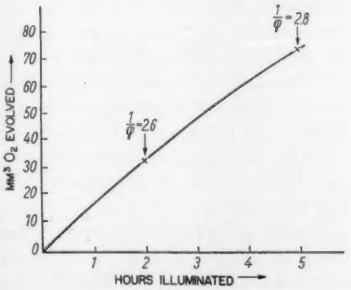

Fig. 3. Oxygen gas produced at constant illumination with green light with a small quantity of blue-green light added (five-hour experiment).

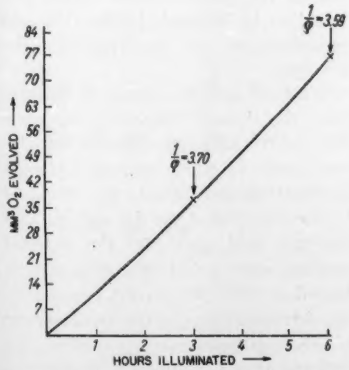

Fig. 4. Oxygen gas produced at constant illumination with green light with a small quantity of blue-green light added (six-hour experiment).

By measuring photosynthesis under special conditions, a splitting of photosynthesis into two reactions was observed: a *light reaction* and a *dark reaction*. Normally these two reactions overlap each other so that one cannot observe each one separately.

In the light reaction, one molecule of O_2 will develop per molecule of chlorophyll, with, however, a quantum requirement, not of 3, but of 1. This at first appears to contradict the laws of energy. However, during the dark period following the end of illumination it can be observed manometrically, under suitable conditions, that two-thirds of the oxygen gas developed during the light period undergoes a back reaction, with restoration of the original condition wherein light can again produce O_2 as before (*5*). Thus, if the light reaction is not considered by itself, but together with the dark reaction, all is in order energetically.

Closer study showed that in the dark reaction the oxygen of carbonic acid was so loosened that, with the help of the energy of respiration, one quantum then sufficed to produce one molecule of O_2. The carbonic acid derivative with the loosened oxygen is probably a peroxide. In order not to go beyond the facts, we may call it the "photolyte" of photosynthesis.

If we write the light and dark reactions of photosynthesis one after the other, we obtain (Chl, chlorophyll):

$$\text{(Light)}\quad 3(\text{ChlCO}_2^*) + 3\text{N}_o h\nu + 3\text{CO}_2 \rightarrow 3(\text{ChlCO}_2) + 3\text{C} + 3\text{O}_2 \quad (1)$$

$$\text{(Dark)}\quad 2\text{C} + 2\text{O}_2 \rightarrow 2\text{CO}_2 + 200{,}000 \text{ cal} \quad (2)$$

$$\text{(Dark)}\quad 3(\text{ChlCO}_2) \rightarrow 3(\text{ChlCO}_2^*) - 200{,}000 \text{ cal} \quad (3)$$

$$\text{(Balance)}\quad 1\text{CO}_2 + 3\text{N}_o h\nu \rightarrow 1\text{C} + 1\text{O}_2$$

The photolyte derivative of carbonic acid is designated by an asterisk, in order to distinguish it from the untransformed carbonic acid. Nothing in this reaction sequence is theory. All has been found experimentally and measured in *living Chlorella*. Reaction 1, the *light reaction*, is measured by the O_2 development and CO_2 consumption in the light. Reaction 2 is measured by the O_2 consumption and CO_2 production in the dark. Reaction 3, in which the bound, inactive carbonic acid is transformed into the photolyte, is measured by the time that elapses until the light is again able to develop as much O_2 as in reaction 1. In our experimental arrangement this recovery period for full light action lasted about 20 minutes, and could therefore be followed very accurately in its time course.

Table 1. Quantum requirement in 23 consecutive experiments (mole quanta absorbed by chlorophyll/mole O_2 developed).

Date (1957)	Quantum requirement
Mar. 1	4.10
3	3.68
5	3.65
6	3.58
7	4.30
14	3.65
21	4.10
22	3.22
25	4.61
27	3.90
29	3.56
Apr. 1	3.49
3	4.75
9	4.26
10	4.65
11	4.30
15	7.51*
17	3.92
23	3.54
24	2.92
25	3.20
26	4.62
May 1	3.90

* This was the single instance of a poor yield.

The photolyte is written as a chlorophyll compound because the quantity of O_2 that the light can develop from the photolyte is equivalent to the chlorophyll content of the cells (*6*). This is important. We now no longer have any need to wonder how it is possible that the light energy is transferred without loss from the chlorophyll molecule to the photolyte molecule, since we now know that the light acts within the same molecule that absorbs it. The light reaction of photosynthesis is thus nothing else than the photodissociation of a pigment, comparable to the photodissociation of carbon monoxide-hemin compounds, and the quantum yield of 1 is almost self-evident.

Upon adding the three equations of the reaction sequence, the photolyte is eliminated, and the net result is the splitting of carbonic acid by 3 quanta of light, which is what one finds experimentally in the balance of photosynthesis.

Nothing seems to be simpler than this solution of the quantum problem. Of the 110,000 calories that are necessary for the splitting of 1 mole of carbonic acid, 70,000 are provided by a respiratory process. The remaining 40,000 calories that the light provides is exactly the amount of energy of 1 mole quanta of red light. All quantum difficulties are thus eliminated.

In order fully to appreciate this solu-

tion, one must reflect that in photosynthesis no energy would be gained, but rather lost, if the energy of the respiratory process were taken from the energy store of the cells. Only because the respiratory energy of reaction 2 is directly supplied by light is a net gain of energy attained. All detail is simple physics and chemistry. But the whole is a higher kind of physics and chemistry, devised by the genius of living nature.

To conclude the discussion of energetics, I would like to describe an experiment that ought to be demonstrated to all students of biochemistry, because it confirms in the simplest possible way the requirement of our equations that there is no photosynthesis without respiration.

Figure 5 shows the experimental vessel that is to be attached to a manometer. The vessel contains *Chlorella* suspended in a carbonate-bicarbonate mixture that maintains the CO_2 pressure constant, so that pressure changes registered by the manometer can only be changes in O_2 pressure. The gas space contains argon and a very little oxygen.

Fig. 5. Vessel for demonstration of the necessity of respiration for photosynthesis.

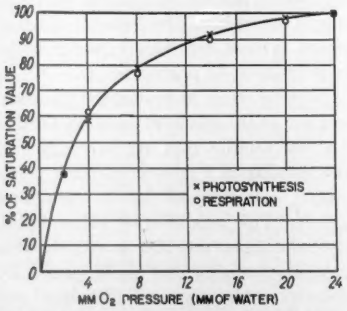

Fig. 6. Respiration and photosynthesis at low pressures of O_2.

The essence of our experimental arrangement is that we employ the cells themselves to attain the desired low O_2 pressures. When we darken the cells the O_2 pressure sinks at once on account of the respiration; and when we illuminate the cells the O_2 pressure rises at once on account of the photosynthesis. This cycle can be repeated as often as desired without opening the vessel. The manometer shows us at any time the prevailing O_2 pressure, and the change in manometer fluid level shows us for any time period of pressure change the respective respiration or photosynthesis. We thus learn whether, and in what manner, respiration or photosynthesis changes as a function of O_2 pressure.

The result is shown graphically in Fig. 6, in which the changes of respiration and photosynthesis are plotted against O_2 pressure. As one sees, both respiration and photosynthesis change with O_2 pressure, and indeed identically. An O_2 pressure of 3 mm of water is the half-saturation value for both processes, and 20 mm yields virtual saturation for both processes. Below an O_2 pressure of 1 mm of water, respiration and photosynthesis are both very small.

The experiment shows much more than that oxygen gas is necessary for photosynthesis. It shows that not merely traces of oxygen are necessary, but definite and easily measurable pressures of oxygen, and that these pressures are necessary because they are necessary for the respiration. All is precisely as our equations demand. *Without respiration, no photosynthesis!*

Chemistry of Photosynthesis

We now leave energetics and turn to the chemistry of photosynthesis. The problems posed here are clearly given by the results of the energetics. What happens chemically to carbonic acid in the dark reaction of photosynthesis? Or, expressed otherwise, what is the photolyte chemically? The gates to this field were opened by the following experiment (7).

The main compartment of a conical manometric vessel (Fig. 7) contains a suspension of *Chlorella*, the side arm contains fluoride, and the gas space contains argon free of CO_2 and O_2. The *p*H of the suspension and of the fluoride is 3.8. Upon tipping the fluoride from the side-arm into the main compartment, a vigorous evolution of CO_2 from the cells takes place. From 100 mm^3 of *Chlorella* cells, 30 to 40 mm^3 of CO_2 will be developed in a few minutes. The content of

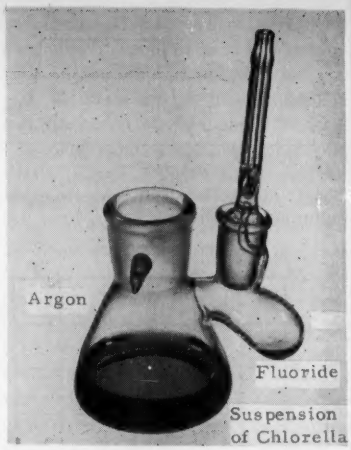

Fig. 7. Vessel for measuring labile CO_2.

this labile CO_2 in *Chlorella* is thus very great—greater, for example, than the content of oxyhemoglobin-O_2 in red blood cells. A trace of cyanide diminishes the development of the CO_2, from which one must conclude that it is an enzymic reaction that is activated by the fluoride.

There are two facts of special interest about the fluoride reaction. First, if one expels the CO_2 with $N/1000$ fluoride anaerobically, and then passes O_2 into the suspension, the expelled CO_2 will for the most part be taken up again. The energy of the respiration induced by the added O_2 is necessary for this rebinding of CO_2. Obviously, the analogy here to the dark reaction in photosynthesis is very far-reaching.

Second, and equally important: if one expels the labile CO_2 from the *Chlorella* with low concentrations of fluoride, and then illuminates, photosynthesis is found to be inhibited; but if one removes the fluoride from the cells by washing, and waits until the CO_2 is again aerobically bound, the photosynthetic capacity is found to be restored. Labile CO_2 and photosynthesis are thus mutually dependent.

We have spared no pains to discover what the chemical source of the labile CO_2 is. We have found that it is L-glutamic acid (*8*), which occurs in *Chlorella* in loosely bound form to the extent of 0.5 to 1 percent of the dry weight. This glutamic acid goes into the external medium when a *Chlorella* suspension is heated at 90°C for several minutes. If one determines the glutamic acid content of the centrifuged external medium *before* and *after* a treatment with fluoride, one finds that as much glutamic acid has disappeared as CO_2 has been developed by the fluoride!

γ-Aminobutyric acid is formed along with the CO_2 in the fluoride reaction. Aerobically, γ-aminobutyric acid and CO_2 react in the cells to yield glutamic acid again, so that aerobically a stationary state is set up between decomposition and resynthesis of glutamic acid:

$$\text{L-Glutamic acid} \rightleftharpoons \gamma\text{-aminobutyric acid} + CO_2$$

The α-decarboxylation of glutamic acid was discovered in bacteria in 1910 by Ackermann and in green plant cells in 1937 by the Japanese Okonuki. Both the decomposition and resynthesis of glutamic acid can be demonstrated when one transfers the heated extracts of *Chlorella* onto chromatograph filter paper, develops with phenol-citrate solution, and sprays with ninhydrin in the standard way.

As known test substances for the chromatogram, we have employed aspartic acid, glutamic acid, alanine, and γ-aminobutyric acid. The experimental runs in Fig. 8 show that under its normal living conditions *Chlorella* contains little aspartic acid, much glutamic acid, much alanine, and no γ-aminobutyric acid. We presume that the glutamic acid is combined with the chlorophyll, since normally cultured cells contain one to two molecules of glutamic acid per molecule of chlorophyll. In *N*/80 fluoride the glutamic acid decreases and appears as γ-aminobutyric acid. This result is obtained both anaerobically and aerobically, since at this high concentration of fluoride no glutamic acid will be resynthesized.

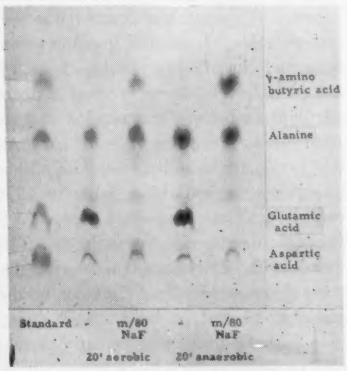

Fig. 8. Action of *N*/80 fluoride: no difference aerobically and anaerobically (phenol-citrate-phosphate; Whatman filter No. 1 unidimensional).

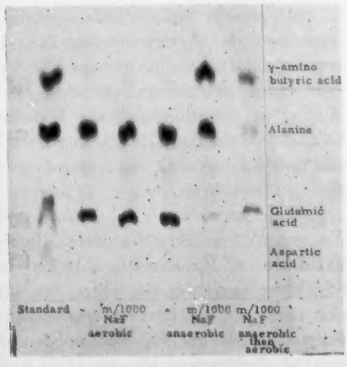

Fig. 9. Action of *N*/1000 fluoride; large difference aerobically and anaerobically (phenol-citrate-phosphate; Whatman filter No. 1 unidimensional).

In the experiment of Fig. 9 the fluoride concentration was only *N*/1000, and here one sees a great difference anaerobically and aerobically. Anaerobically the decomposition is very extensive, but aerobically it is small.

The more the glutamic acid is destroyed, just so much the more is the photosynthesis inhibited. For example, two different concentrations of fluoride were added to aliquot *Chlorella* suspensions under aerobic conditions, and the glutamic acid content and photosynthesis measured. Table 2 shows how closely decomposition of glutamic acid and inhibition of photosynthesis parallel each other.

Continuation of these experiments brought forth a further connection between glutamic acid and CO_2. A study of the binding of CO_2 by *Chlorella* at different pressures of CO_2 showed that the labile CO_2 is not only bound as the α-carboxyl of glutamic acid but in addition an equal quantity of CO_2 is dissociably bound under aerobic conditions. This dissociable CO_2 is also given off when the glutamic acid in the cells is decomposed. The saturation value of the dissociating CO_2 is very nearly equal to the glutamic acid content of the cells. The formation of carbamino-glutamic acid is perhaps involved in the dissociable complex.

In conclusion I may mention further that we have begun to study the behavior of amino acids in photosynthesis with the help of radioactive CO_2. The main compartment of a manometric vessel (Fig. 10) is filled with a suspension of *Chlorella*, the Siamese side arm in one part with C^{14}-carbonate and the other part with excess lactic acid. Upon tipping the acid onto the carbonate, a pressure of radioactive CO_2 is obtained in the gas phase. Vessels so prepared were illuminated ½, 1, or 5 minutes and then, along with dark control vessels, immersed in hot water in order to stop all enzymatic reactions and at the same time

Fig. 10. Manometric vessel for experiments with radioactive CO_2.

extract the soluble materials from the cells. After centrifugation, the heated extracts were chromatographed in two dimensions, and measurements were made with a Geiger counter.

It can be seen from Table 3, first, that the amino acids, alanine and aspartic acid, rapidly became radioactive—indeed, more rapidly than the phosphorylated glyceric acid, contrary to previous reports in the literature for experiments of this general type. Second, the table shows that aspartic acid and alanine become radioactive more quickly than glutamic acid, so that one can think that an alanine-aspartic acid system enters before the glutamic acid system. Manometric experiments alone have not as yet given any such indication, and one must wait until combined radiometry, manometry, and bolometry have become so far developed quantitatively that one can draw more certain conclusions. Radiometry alone has already led to a multiplicity of errors.

Summary

With the establishment of conditions for optimum culturing and measurement, there is now final proof that in photo-

Table 2. Comparative action of fluoride on decomposition of glutamic acid and on inhibition of photosynthesis.

Fluoride concentration	Decomposition of glutamic acid (%)	Inhibition of photosynthesis (%)
N/640	21	18
N/320	64	64

Table 3. Geiger counter impulses per minute by chromatographed heated extracts of 10 mm^3 of *Chlorella* cells.

Amino acid or other material	Geiger counter impulses per minute					
	10 min dark, 0.5 min dark	10 min dark, 0.5 min light	5 min dark, 1 min dark	5 min dark, 1 min light	5 min dark, 5 min dark	5 min dark, 5 min light
Aspartic acid	8520	18750	9320	14205	8000	30100
Glutamic acid	1136	1614	1096	1900	3350	17000
Alanine	710	6950	940	19000	817	37500
Phosphorylated sugar and glyceric acid	95	3451	147	9800	523	23800
Nonphosphorylated sugar	Not determined		143	113	857	2726

synthesis at high as well as low light intensities the light energy can be almost completely converted into chemical energy. There is thus drawn to a close an investigation that was initiated many years ago in Berlin in the Imperial Institute of Physics (*9*).

The second result is the establishment of a general physical mechanism of photosynthesis, involving an interplay between light energy and respiratory energy, and therewith the solution of the quantum problem in photosynthesis.

The third result is the establishment of the function of chlorophyll as a stoichiometric, chemically reacting component in photosynthesis.

There remains the special chemistry of photosynthesis. In this still-unfinished field of investigation, the latest discovery is the labile carbon dioxide of *Chlorella*, connected with the decomposition and resynthesis of glutamic acid in living *Chlorella*, and connected with the possible function of the amino acids, aspartic and glutamic, in the binding and reduction of carbonic acid. The dissociating CO_2 is bound by *Chlorella* only in the presence of O_2 and of cellular glutamic acid. This CO_2 is released if the oxygen pressure is lowered below 2 mm of water or if—in the presence of oxygen—the glutamic acid is split in the living *Chlorella*, for example, by $N/10,000$ benzoquinone. This is the CO_2 that is used in light and taken up in the dark (*8*).

Remarks

1) *Quantum requirement in the United States.* In the years 1938 to 1948 the quantum requirement of photosynthesis was measured in various institutes in the United States with the result that 12 to 20 quanta were found to be required by *Chlorella* for the development of one molecule of O_2. The average value was 16. The value of 12 was regarded as the optimum value. A few, including Dean Burk and van Niel, dissented, but the interpreters and advocates of the high quantum numbers, James Franck and Eugene Rabinowitch, maintained the upper hand. In 1941 Franck and Gaffron (*10*) wrote, "*We know now that the high efficiency is only apparent and that the true efficiency is probably only a third of it, namely 12 quanta per molecule CO_2 reduced*" (italics added). The "photosynthetic unit" in Urbana, Emerson and Rabinowitch, stayed with the high quantum numbers until at least 1952 (*11*). Later, under the influence of the Dahlem investigations, the quantum numbers reported in the United States sank, and today approach the Dahlem number of 4 to 3 (*12*).

2) *Light reaction and dark reaction.* According to the equations of the light and dark reactions, which can be separated in point of time, CO_2 is taken up anew in the light reaction, so that the ratio CO_2/O_2 is about -1 in the light reaction per se (although the CO_2 from which the oxygen is developed may not be the CO_2 that is taken up). However, this holds only for optimally cultured cells whose quantum requirement in the balance is 3 to 4. Other cells, for example those grown at a south window with added constant artificial illumination, may take up CO_2 more slowly, so that the ratio CO_2/O_2 in the light reaction is not -1 but lies between -1 and 0. In the latter extreme the new CO_2 is first taken up in the dark reaction following cessation of illumination. Thus there are two reactions of CO_2 to be distinguished: the binding of CO_2, and the transformation of bound CO_2 into the photolyte. In the case of optimally cultured cells, these two reactions of CO_2 may be completely separated, whereas the O_2 development and the binding of CO_2 take place simultaneously and equally. In the less active cells the two reactions of CO_2 are not separated in time, whereas O_2 development and CO_2-binding are separated. The unraveling of these relations has cost many experiments.

3) *The unit of 2500 chlorophyll molecules.* In 1932 Emerson and Arnold (*13*) attempted to apply our methods of intermittent illumination (*14*) to photosynthesis. For example, with very short, very bright light flashes and relatively long dark periods, they determined the maximum quantity of O_2 that appeared to be developed in *one* light flash. Comparison of this quantity of O_2 with the chlorophyll content of the cells showed that 2500 molecules of chlorophyll could develop *one* molecule of O_2. In contrast, we find, without intermittent light, and with direct measurement of the light reaction during inhibition of the dark reaction, that *one* molecule of chlorophyll can develop *one* molecule of O_2. There is thus a discrepancy of three powers of 10, depending upon whether the ratio chlorophyll/oxygen is measured with intermittent light or directly. As Dean Burk (*15, 16*) has shown, however, the intensity of the light flash in the experiments of Emerson and Arnold was several orders of magnitude too low—that is, entirely insufficient—to decompose all the photolyte in the very short time of the light flash ($\sim 10^{-5}$ second).

4) *Burst of carbon dioxide.* According to Emerson and Lewis (*17*), photosynthesis begins with a burst of CO_2 evolution. This phenomenon was discovered manometrically with the two-vessel method, without, however, maintaining the essential requirement of the method. Instead of both vessels being illuminated simultaneously, an interval of 8 to 24 hours took place between illumination of one vessel and the other. This procedure removed the essential condition of the two-vessel method, namely, that in the two unequal vessels the same chemical change must occur. If one properly measures, as nowadays prescribed, the O_2 development in both vessels simultaneously with a divided light beam, one never finds at the beginning of the illumination a burst of CO_2 out of the living cells, but always and only a burst of O_2, corresponding to true photosynthesis.

5) *The experiments of Ruben and Kamen.* When *Chlorella* were illuminated in a bicarbonate solution in which the oxygen of the water, but not that of the carbon dioxide, was isotopically marked, the O_2 developed was marked. Ruben and Kamen (*18*) concluded that the light decomposed primarily the H_2O but not the CO_2. Obviously this conclusion would have been

correct only if one could have brought forth the improbable argument that in light not the hydrate but only the anhydride of carbon dioxide reacted.

6) *"Hill" reactions.* If one suspends *Chlorella* cells in nitrate-nitric acid mixture, the cells develop O_2 for many hours when illuminated in the absence of CO_2, according to the equation

$$HNO_3 + H_2O = NH_3 + 2O_2,$$

a reaction that was discovered in 1920 (*19*). The mechanism of this reaction has been clarified as follows: the nitric acid oxidizes in a dark reaction the carbon of cell organic matter to carbon dioxide, and then, in light, splitting of the carbon dioxide into C and O_2 occurs, as in ordinary photosynthesis:

(Dark) $HNO_3 + 2C + H_2O = NH_3 + 2CO_2$
(Light) $2CO_2 = 2C + 2O_2$
(Balance) $HNO_3 + H_2O = NH_3 + 2O_2$.

In 1955 we found (*20*) that one can replace the nitric acid by ferricyanide:

(Dark) $4Fe^{3+} + C + 2H_2O = 4Fe^{2+} + 4H^+ + CO_2$
(Light) $CO_2 = C + O_2$
(Balance) $4Fe^{3+} + 2H_2O = 4Fe^{2+} + 4H^+ + O_2$.

Both reactions, with living *Chlorella*, appear in the balance as though water were decomposed by light, and as though the oxidizing agent acted only as a hydrogen acceptor, whereas in reality the light reaction is ordinary photosynthesis.

If, in the experiments with living *Chlorella*, one substitutes quinone for the nitric acid or the ferricyanide, CO_2 cannot participate in the development of O_2, since quinone completely inhibits the splitting of CO_2. Likewise, with green grana, CO_2 cannot participate in the development of O_2 since illuminated green grana are unable to reduce CO_2.

One must therefore either postulate two different mechanisms of photochemical O_2 development in green grana and in intact cells, which is improbable, or one must attempt to find a common explanation for the two phenomena: for water decomposition with intermediate photosynthesis, and for water decomposition without intermediate photosynthesis (*6*).

7) *The experiments of F. W. Allen.* In order to test whether photosynthesis without O_2 is possible, Allen (*21*), at the suggestion of James Franck, made use of the fact that the phosphorescence of many dyes is diminished by traces of O_2. A stream of nitrogen containing CO_2 was conducted over glowing copper, from there over water, then over a suspension of *Chlorella*, over liquid nitrogen, and finally over the dye acriflavin adsorbed on silica gel. Allen still found detectable photosynthesis at an O_2 pressure of 10^{-6} mm-Hg; whereas our manometry in closed vessels showed, without possibility of error, that below 10^{-1} mm-Hg photosynthesis in *Chlorella* is very small. What is the meaning of this discrepancy of five powers of 10?

The method of James Franck must be calibrated empirically—that is, each O_2 pressure yielding a given phosphorescence must be analytically determined. Furthermore, O_2 pressures of the order of magnitude of 10^{-6} mm-Hg must be produced, maintained, and analytically measured in a rapidly flowing gas. Anyone who is accustomed to performing experiments himself knows that this is an almost insoluble task. In any event, the analytical determination of traces of O_2 is the key aspect of the Franck method, and since Allen himself remained silent about this point, one must seek the mistake here. The calibration was obviously false by five powers of 10.

On the other hand, experiments of Hill and Whittingham (*22*) agree very well with our results. These workers added reduced hemoglobin to a suspension of *Chlorella* and determined the O_2-development upon illumination by optical measurements of the resulting oxyhemoglobin. They found that photosynthesis already began to fall off at an O_2 pressure of about 2 mm-Hg.

8) *The experiments of Allan Brown on "light-respiration."* When the light reaction and the dark reaction overlap in photosynthesis under normal conditions, two-thirds of the O_2 developing in the light will be reabsorbed so rapidly that one can think of the oxygen as oscillating between the free state and a binding with carbon. If the molecular O_2 provided the *Chlorella* is isotopically marked, whereas the CO_2 provided is not marked, one cannot expect that more marked O_2 will be consumed in light than in darkness, since in light, on spatial grounds, the unmarked O_2 photosynthetically produced within the cells will be consumed more rapidly than the externally available marked O_2 that must diffuse into the cells. Brown (*23*) found, in fact, that in light there was no increase in marked respiration, but often even a decrease of marked respiration; that is, not only the light respiration but also the dark respiration favored the unmarked oxygen produced within the cells photosynthetically from unmarked photolyte. This is a beautiful example of "isotopic discrimination."

The light respiration during illumination has also been the object of attempted measurement elsewhere, for example by Weigl, Warrington and Calvin (*24*), who illuminated green cells in marked CO_2 and expected that in light unmarked CO_2 would be given off in increasing quantity. They found, however, no increase in unmarked CO_2, quite in agreement with our equations, from which it follows that the light respiration must be marked when the CO_2 is marked.

In fact, the light respiration can only be measured as it was first discovered (*4*): when it is separated in time from O_2 development (*25, 26*).

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K. N. Kornilov, Theoretical and Experimental Psychologist

Konstantin Nikolayevich Kornilov was born in Siberia, 9 March, 1879. He died in Moscow, 10 July, 1957. An idealistic populist (in Russian, *Narodnik*) in his youth, he did not enter a university until after he had paid his debt to society and contributed to the education of the masses by teaching elementary school for several years. He was graduated from the Historico-Philological Faculty of Moscow University in 1910 and was retained at the university as an assistant to G. I. Chelpanov, the leading Wundtian experimental psychologist in pre-Soviet Russia. Kornilov's research interests turned quickly to the study of simple reactions, which he investigated, by means of a specially constructed dynamoscope, with respect not only to speed but also to force and form of movements. Varying the types of reactions and correlating physical measurements with types and with his subjects' introspections, Kornilov arrived at the view that the "product of expenditure of physical and mental energy in human reactions is a constant" and, generalizing, that "mental processes are inhibited will reactions."

After the Revolution, Kornilov's first publications were in the immediate area of service to educational psychology. Yet he continued experimenting intensively on reactions in the laboratory, finally raising such studies to the status of an all-embracing school of psychology, named reactology. "Psychology is the science of the reactions of the individual: their chronometry or speed; their dynamometry or force; their 'motographics' or extent, rate, and form; their psychological complexity [a hierarchy of seven reactions was noted]; their contents or social import; and their inter- and intra-individual differences." To these were added (i) wholeness (in Russian, *Tselostnost'*): organismically, total behavior dominates individual-reaction behavior and, societally, "we must always proceed, not from individual to social psychology, but from social and class psychology to group, occupational, and individual psychology"; and (ii) economic prepotency: "the social aspects (the contents) of man's reactions are a variate function of a particular economic class."

Kornilov's reactology, represented as a Hegelian synthesis of behavior and consciousness psychologies, reflexes and *Bewusstseinslagen*, will and determinism, holism and atomism, and quantitative and qualitative emphases and, allowing generously for Marxian economics, quickly became the dominant school of psychology in the Soviet Union of the 1920's. His *Textbook of Psychology from the Standpoint of Dialectical Materialism* went through five Russian editions between 1926 and 1931 and was translated into a number of languages. He became the director of the country's most important research center, the Moscow Institute of Psychology, in 1923, and the editor of Russia's first pure (unhyphenated) psychological periodical, *Psikhologiya,* in 1928.

However, quick as the rise of reactology was, its demise was even quicker. Soon after the publication of Lenin's *Philosophical Notebooks* (his marginal comments on the philosophical books that he read), in 1929–1930, the Communist cell of the Moscow Institute of Psychology initiated a series of intensive discussions of the basic premises of reactology and reached negative conclusions. The exact text of the discussions and criticisms was not published, but later articles indicate that the charges revolved around the following points. (i) Man as a mere reacting organism is too passive a conception for the actionism of Lenin and Marx and Engels. (ii) The view that the physical and the mental (or the peripheral and the central) in human reactions complement each other implies that psychical processes are "the other side of *physiological* processes," whereas the Leninist position is that the "psyche and consciousness are true reflectors of objective *physical* reality." (iii) Reactology leads to either psychophysical parallelism or epiphenomenalism—the first, reactionary-idealistic, the second, vulgarly mechanistic, and both failing to accord to consciousness its proper activist Leninist role in transforming nature, man, and society. (iv) In practice, reactology has become a variety of behaviorism, and behaviorism is essentially a school in the service of American capitalism—a psychology of man as an automaton permitting more ruthless exploitation and more deceitful decoying of the working class (sic!). At any rate, beginning with 1931, reactology disappeared wholly from Soviet psychological writings, not excepting the writings of Kornilov himself.

Kornilov, however, remained a leading —though no longer *the* leading—figure in Soviet psychology. He lost the directorship of the Moscow Institute of Psychology but continued as editor of *Psikhologiya,* became dean and later head of the department of psychology of the Moscow State Institute of Pedagogy, and was elected vice president of the Soviet Academy of Pedagogical Sciences (established in 1943). Moreover, he continued to contribute a considerable number of significant articles on psychological theory and practice to a variety of Soviet periodicals and continued as a prolific writer of textbooks, which in terms of Soviet psychology, it must be remembered, is a high honor and distinction. His *Psikhologiya* (with Teplov and Shvarts) came out in 1938 (second edition in 1941); *Psikhologiya* designed for secondary schools and printed in an edition of 100,000 copies, was published in 1946; and *Psikhologiya* (with Smirnov and Teplov), which for a number of years was the country's sole college textbook in the field, came out in 1948. Kornilov became the editor of *Semya and Shkola* ("Family and School") in 1946 and a member of the editorial board of *Voprosy Psikhologii* in 1955 (the year of its founding).

The last article by Kornilov that I read appeared in the 1955 July–August issue of *Voprosy Psikhologii* under the title of "Problems of Soviet psychology." The article is strikingly reminiscent of one he wrote in 1925, under the title of "Psychology and Marxism." Soviet psychology has in these 30 years passed through a complete evolutionary cycle—or an expanding Hegelian helix, they might say. It has returned to Pavlov! Accordingly, as in 1925, Kornilov sets out to argue that psychology must not and could not be liquidated by physiology, that it has its own specific scientific laws and methods, and that the unity of the brain and mind does not mean identity. Moreover, though this time Kornilov pays unmis-

takable tribute to the correctness of Pavlov's laws of higher nervous activity, he is, on the other hand, more explicit in his claims that human psychology has supraphysiological status, that it is more a social than a biological science, and that its key concept of human personality involves sociohistorical as well as psychological and physiological factors. Kornilov's concern with basic problems of Soviet psychology was indeed a matter of life-long dedication. And—this should be especially noted—he somehow managed at all times to keep afloat, in fact to be most of the time in the forefront, untoward and adverse trends to the contrary notwithstanding. Soviet sources have it that Kornilov was not a member of the Communist party.

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News of Science

United States Euratom Program

On 23 June the President transmitted to Congress an international agreement between the United States and the European Atomic Energy Community (Euratom). Under the United States Atomic Energy Act, Congressional approval of this instrument is necessary prior to entering into a U.S.–Euratom agreement for cooperation which would embrace a 1-million-kilowatt joint program of nuclear power development.

This program involves the construction by 1963 in the six Euratom countries—Belgium, France, the Federal Republic of Germany, Italy, Luxembourg, and the Netherlands—of approximately six large-scale nuclear power plants based on United States type reactors. This would provide sufficient electrical generating capacity to meet the power requirements of more than 5 million people in the Euratom area. An outline of the proposed United States–Euratom program follows.

Objectives. The aim of the joint program will be to bring into operation in the Community by 1963 about 1 million electric kilowatts of installed nuclear capacity, in reactors of proven types developed in the United States, and to initiate immediately a joint research and development program centered on these reactors. The program would be conducted so as to obtain maximum support of the industries of the Community and of the United States. The active participation of industries is indispensable to the success of the program.

Capital costs. The total capital cost, exclusive of fuel, is estimated not to exceed $350 million. These funds will be provided by the participating utilities and other European sources of capital, such financing to be arranged with the appropriate assistance of Euratom. Up to $135 million would be provided by the United States Government to Euratom in the form of a long-term line of credit from the Export–Import Bank. These funds will be re-lent by Euratom for the construction of nuclear power plants.

Operation of plants. The nuclear power plants will be built, owned, and operated by utilities in the member states. All risks due to uncertainties in construction, maintenance, and operating costs and load factors will be borne directly by these utilities. In the course of the negotiation it was determined that the economic risks associated today with the reactor fuel cycle must be minimized if participation by the European utility industry is to be assured. To this end, the United States, for a 10-year period of operation, will guarantee ceiling costs for the fabrication of the fuel elements required, as well as a fixed life for these elements.

Research program. A research and development program, established for a 10-year period, will be centered on improvement in the performance of the reactors and the lowering of fuel cycle costs. During the first 5 years, the financial contribution of the Community and the United States will amount to about $50 million each, with the sum required for the second 5-year period to be determined at a later date.

Fuel requirements. Under the arrangements proposed, the United States would sell to the Community a net quantity of 30,000 kilograms of contained U^{235} in uranium to cover the fueling and other requirements of the program for such material over a 20-year operating period. The initial operating inventory, which amounts to approximately 9000 kilograms of contained U^{235}, would be sold to the Community on a deferred payment basis. The balance of about 20,000 kilograms—which represents estimated burn-up and process losses over the 20-year period, and 1000 kilograms to provide for research and test reactors associated with the program—would be paid for on a current basis.

The U.S. Atomic Energy Commission will process in its facilities, at established U.S.–domestic prices, spent fuel elements from the reactors to be included in the program.

Special nuclear materials. With respect to any special nuclear material produced in reactors fueled with materials obtained from the United States under this joint program, which is in excess of the need of the Community for such material for the peaceful uses of atomic energy, the International Atomic Energy Agency would have the right of first option to purchase such material at the announced fuel value price in effect in the United States at the time of purchase. In the event this option is not exercised by the agency, the United States would be prepared during the first 10 years of reactor operation to purchase such material at the U.S.-announced fuel value price in effect at the time of purchase.

Data exchange. Technological and economic data developed under the program would be made available to the industries within the Community and the United States under provisions designed to assure the widespread dissemination of the information developed in the course of the program.

Safeguards system. Under the program the Community will assume responsibility for the establishment of a safeguards system which will be formulated in accordance with agreed upon principles. This system will be designed to assure that the materials received from the United States, as well as special nuclear material produced therefrom, will be used only for peaceful purposes. The proposed agreement for cooperation with the Community provides that there will be frequent consultation on the operation of the system. Continuation of the cooperative program will be contingent upon the Community's establishing and maintaining a mutually satisfactory safeguards system.

The Community also has agreed to

consult with the International Atomic Energy Agency to assure the development of a safeguard system reasonably compatible with that of the agency. In addition, in the event of the establishment of an international safeguards and control system by the International Atomic Energy Agency, the United States and Euratom will consult regarding assumption by that agency of the safeguards and control over fissionable material utilized and produced in implementation of the joint program.

Basic Curriculum Study

How much should a student know about himself and his world after 12 years of schooling? In an attempt to find an answer, the Council for Basic Education, Washington, D.C., has brought together a group of men and women representing many agencies concerned with the problem. The council, headed by Howard A. Meyerhoff, president, has received a grant of approximately $34,000 from the Relm Foundation, Ann Arbor, Mich.

The council's planning group met recently to discuss the first phase of a "Basic Curriculum Study"—a study divided into four phases from which will come, over a period of several years, a series of publications dealing with the basic curriculum, with the preparation of teachers, with the gifted child, and with a system of national academic achievement examinations. Each publication will be the subject of a national conference, the first one to be held next fall in Washington, D.C.

At that meeting an effort will be made to define the level of attainment that graduating high school students should reach in what the Council calls the basic subjects: English, history, foreign languages, geography, mathematics, biology, chemistry, and physics. An outstanding scholar in each subject will present a paper describing, for his particular field, the proper educational aims of the public school. The papers will be published subsequently in the form of a citizen's handbook that will be made widely available.

Conservation Slide Rule

Research data on soil conservation, gathered by U.S. Department of Agriculture scientists over the past 30 years, is now readily available for practical use by technicians in the form of a simple conservation slide rule that makes possible fast and reliable soil-loss estimates right in the field. This slide rule, developed from information compiled by scientists of USDA's Agricultural Research Service, is in use by soil-conservation technicians in the nine Corn Belt States to help farmers protect their land. It was designed by J. J. Pierre of the Soil Conservation Service, using information previously available to soil conservation technicians only in tabular and chart form. Although the present slide rule is adapted only to Kentucky, Minnesota, Iowa, Missouri, Wisconsin, Illinois, Indiana, Ohio, and Michigan, research information is being developed to make similar prediction methods available to soil conservation technicians in other parts of the United States.

Since 1929, soil and water conservation experiment stations throughout the country have been studying the most important factors governing the amount of soil and water lost from farmland during rainstorms. All these factors except rainfall itself are influenced to some extent by the method of cropping and conservation practices used.

The rate of erosion caused by storms depends on the force with which raindrops stir up soil and the amount and speed of the runoff water. Erosion is also affected by the kind of soil, kind and amount of soil cover, and steepness and length of slope, as well as soil-management and conservation practices. When enough experimental data are available to give accurate relative values for these various factors, mathematical methods can be used to estimate or predict soil loss on a particular farm.

Medical Research in Australia

Last March Sir Howard Florey, in the presence of the Prime Minister of Australia, opened the new building of the John Curtin School of Medical Research at the Australian National University in Canberra. The National University was founded in 1946 as a national center for research and research training, initially in the fields of physical sciences, medical sciences, and the social sciences.

There had long been complaints in Australia that many of the most able scientists left the country because of the greater attractions in universities and research institutions in Great Britain. Such complaints applied more to the medical sciences than to other natural sciences, for which the large and varied laboratories of C.S.I.R.O. provided first-class facilities, whereas the only medical research institute in Australia with an international reputation was the relatively small Walter and Eliza Hall Institute in Melbourne.

In a report to the Commonwealth Government in 1944, Florey suggested that a national institute for advanced medical sciences should be set up in Australia, and the John Curtin School of Medical Research, established as an integral part of a university devoted to research and research training, is the result of this suggestion. Florey was intimately associated with the development of the school from the time of his report until 1955, and the building he opened in March is a monument to his inspiration and drive.

There were no laboratories in Canberra in 1948 when the first professor was appointed, so the departments were started in laboratory space lent by several institutions—biochemistry at the Commonwealth Serum Laboratories, Melbourne; medical chemistry at the Wellcome Research Institution in London; microbiology at the Walter and Eliza Hall Institute in Melbourne; experimental pathology in Florey's laboratories in Oxford; and physiology in the University of Otago in New Zealand.

In 1951 temporary laboratories were built in Canberra. These were occupied between 1952 and 1957, when the departments were transferred to the present building, a brick structure of about 170,000 square feet in floor area. At present the total research staff is about 40 and there are some 20 Ph.D. students.

Research Institutes in the U.S.S.R.

A revised *Directory of Medical and Biological Research Institutes of the U.S.S.R.* has been issued by the National Institutes of Health, Public Health Service. The 1958 *Directory* lists more than 700 institutes with their subdivisions, and includes a general subject and name index. Its purpose is to facilitate the exchange of scientific information between the United States and the U.S.S.R., to provide materials for study of the organization of Russian biomedical research, and to assist scientists in planning visits to Russian research centers.

A limited supply of the 1958 edition (PHS Publication No. 587) is available. Requests for single copies should be addressed to the Publications and Reports section, Scientific Reports Branch, National Institutes of Health, Bethesda 14, Md.

Mental Health

Plans for a World Mental Health Year in 1960 sponsored by 108 mental health and professional societies in 43 countries and territories have been announced by the New York Office of the World Federation for Mental Health. Following the pattern of the International Geophysical Year, the purpose of the program is to stimulate mental health activities, including research, with a maximum of international cooperation. The federation, a non-governmental or-

ganization which includes 29 societies in the United States and 79 in 42 other countries, reports a world-wide increase in work for the promotion of mental health during the 10 years since it was organized, not only in countries where it has member societies, but in a number of others with which it has no formal link.

Five major mental health objectives have been singled out for intensive effort: (i) to increase the study of child development in different countries; (ii) to increase the knowledge of the many causes and the distribution of mental illness; (iii) to improve and extend the teaching of the principles of mental health in medical and nursing schools, teacher training colleges, schools of social work, theological seminaries and similar centers of professional training; (iv) to develop knowledge and techniques for dealing with the human relations problems which arise in industries and all types of occupations; and (v) to encourage the study and creation of better methods of preventing and dealing with psychological problems arising from migration within and between countries, whether voluntary or involuntary.

In addition to the major objectives, each country is being encouraged to develop more extensive national programs, particularly in those aspects having areas of special local significance. The United States, with its 29 member societies, will conduct a program on a larger scale than most other countries. To coordinate activities in the U.S., a steering committee has been named as follows: Marian J. FitzSimons, Frank Fremont-Smith, John P. Gillin, Alberta Jacoby, Marian McBee, Mabel Ross, Ruth Simonson, George S. Stevenson and Mottram P. Torre.

Responsibility for financial support of plans and projects within the United States has been assumed by the World Federation for Mental Health: United States Committee, Inc. This committee, formerly known as the International Committee for Mental Health, was founded by Clifford Beers in 1930. Its present officers are: Mrs. Clifford W. Beers, Earl D. Bond, Arthur H. Ruggles and Mrs. Henry Ittleson, honorary presidents; Mrs. Charles S. Ascher, president; Mrs. Jonathan Bingham and John A. P. Millet, vice presidents; Frank Fremont-Smith, general secretary; and George S. Stevenson, treasurer.

Grants, Fellowships, and Awards

General. Applications will be accepted through *15 October* by the National Science Foundation for both the senior postdoctoral and science faculty fellowships. Henceforth, these fellowships will be awarded annually in December rather than biannually as awarded in previous years. Awards will be made in the mathematical, physical, and engineering sciences; medical and biological sciences, including anthropology and psychology (excluding clinical psychology); and in selected fields of social science. Included as well are interdisciplinary fields which overlap two or more scientific disciplines.

To be eligible for senior postdoctoral fellowships, candidates must be citizens of the United States with special aptitude for advanced training, and must have held the doctoral degree for at least 5 years or have equivalent education and experience.

The science faculty fellowships are directed toward college teachers of science who wish to improve their competence as teachers. These fellowships are open to any citizen of the United States who holds a baccalaureate degree or its equivalent, has demonstrated ability and special aptitude for science teaching and advanced training, and has taught at the collegiate level as a full-time faculty member for not less than 3 years, and intends to continue teaching.

Annual stipends to a maximum of $12,000—adjusted to match as closely as feasible the regular salaries of the recipients—will be awarded under both these programs. Fellows may engage in study or research at any accredited nonprofit institution of higher learning in the United States or at any similar institution abroad approved by the National Science Foundation. A limited allowance to aid in defraying the cost of travel for a fellow and his dependents will also be available. Application materials may be obtained from the Division of Scientific Personnel and Education, National Science Foundation, Washington 25, D.C.

Science teaching. The National Science Foundation has announced that proposals will be accepted *until 1 September* from colleges and universities for the support of 1959–60 Academic-Year Institutes. These institutes offer full-time work in science and mathematics through programs designed especially to improve the quality of instruction offered by high school science and mathematics teachers. Directions for preparing proposals and forms to be used in making application may be obtained by interested institutions of higher education from the Division of Scientific Personnel and Education, National Science Foundation, Washington 25, D.C.

Foundation grants will provide support for 19 Academic-Year Institutes during the 1958–59 school year starting in September. It is expected that grants will be awarded for about 30 institutes for the 1959–60 school year. Each institute provides instruction for about 50 teachers. Foundation grants enable the sponsoring institutions to offer stipends up to $3000 plus additional allowance for dependents and travel. Grants also cover tuition and fees, an allowance for books, and operating costs beyond those supported by tuition payments.

Foundation grants extend complete freedom to sponsoring institutions to administer and conduct their respective programs, and teachers seeking training offered by Academic-Year Institutes should apply directly to the sponsoring college or university, not to the foundation. Most institutions will provide for an additional closely allied summer program which may enable many participating teachers to earn graduate degrees.

Social science. The next closing date for receipt of proposals in the Social Science Research Program of the National Science Foundation is *1 October.* Proposals received by that date will be evaluated in the fall. Approved grants will be activated in time for work to begin in the second semester or the summer of 1959. The Social Science Research Program supports basic research in anthropology, archeology, demography, human ecology, economic and social geography, economics, social psychology, sociology, and history and philosophy of science.

Proposals received after 1 October will be reviewed following the winter closing date of 1 February 1959, with activation of approved grants in the summer and fall of 1959. Inquiries should be addressed to the National Science Foundation, Washington 25, D.C.

Population Trends

The newly published United Nations *Demographic Yearbook* for 1957 reports that the population of the world is increasing at an average rate of 5400 persons every hour, or 47 million a year, a rate that is calculated to double the estimated world total of 2737 million inhabitants within the next 40 years. United Nations statisticians have estimated the world birth rate at 34 per 1000 inhabitants and the death rate at 18. During the past 20 years the death rate has declined well over 25 percent in most countries and as much as 50 percent in several. And since the birth rate has remained high and unchanged in most of these same countries, the world population has increased almost 25 percent in one-fifth of a century. Other information contained in the annual statistical publication is as follows:

Percentagewise, Latin America is the fastest growing area of the world, with an estimated population increase of 2.5 percent annually, as against a world aver-

age of 1.6 percent. Numerically, Asia leads the world with some 24 million additions annually.

Children born in the Netherlands have a longer life expectancy than anywhere else in the world—71 years for males, 74 for females. India, on the other hand, has the shortest life expectancy—32 years for both males and females.

Among men up to the age of 45, accidents, and especially motor vehicle accidents, constitute one of the leading causes of death. Luxembourg leads all other countries in the number of deaths from motor accidents—28.5 per 100,000.

Between the ages of 45 and 64 cancer is the leading cause of death for both men and women in all countries for which statistics are available.

The 664-page *Yearbook* has been compiled by the U.N. Statistical Office on the basis of information received from governments. The new issue features mortality statistics by age, sex, occupation, cause, and so forth. In addition, the *Yearbook* shows the population of every part of the world and the percentage of its increase since 1953, the population density, birth rates, marriage rates, divorce rates, life expectancy, and migration statistics. Since the data coming from advanced and less well developed areas are of unequal quality, they contain weaknesses. Nevertheless, they reveal the problems which must be solved to bring economic and social development abreast of population growth.

New Journals

New Zealand Journal of Geology and Geophysics, vol. 1, No. 1, Feb. 1958. Mabel Rice, Ed. New Zealand Department of Scientific and Industrial Research, Box 8018, Wellington, N.Z. Bimonthly. 30s.

New Zealand Journal of Science, vol. 1, No. 1, Mar. 1958. Mabel Rice, Ed. New Zealand Department of Scientific and Industrial Research, Box 8018, Wellington, N.Z. Quarterly. 20s.

Revista del Servicio Nacional de Salud, vol. 1, No. 1, Oct. 1956. Guillermo Valenzuela Lavin, Ed. Servicio Nacional Salud, Santiago, Chile. Bimonthly. $6.

Revista de la Sociedad Cubana de Historia de la Medicina, vol. 1, No. 1, Jan.–Mar. 1958. Horacio Abascal, Ed. Sociedad Cubana de Historia de la Medicina, Academia de Ciencias, Habana, Cuba. $2.

Technical Progress Review, vol. 1, No. 1, Mar. 1958. U.S. Atomic Energy Commission, Washington, D.C. Quarterly. $2. (Order from Superintendent of Documents, Government Printing Office, Washington 25.)

Vigyan Shikshak, The Science Teacher, vol. 1, No. 1, Jan. 1957. V. N. Wanchoo, Ed. All India Science Teachers' Association, New Delhi 8, India. Quarterly. $2.

WEAR. An international journal on fundamentals of friction, lubrication, wear, and their control in industry, vol. 1, No. 1, Aug. 1957. G. Salomon, Ed. Elsevier, Amsterdam and New York. Bimonthly. $15.

What's New in Agriculture, vol. 1, No. 1, Apr. 1958. G. W. Stamm, Ed. Farm Science Syndicate, Evanston, Ill. Biweekly. $15.

News Briefs

The Atomic Energy Commission and the Department of Defense have announced that the demonstration program for U.N. scientific observers of U.S. progress in reducing radioactive fallout in proportion to total yield of nuclear weapons may be expected to begin no earlier than 3 August and probably will start 10 August. The detonation that is to be a central feature of the demonstration has been designated by the code name Pinon.

* * *

National surveys of laboratory animals are being completed by the International Committee on Laboratory Animals which met recently at Unesco House in Paris. The committee, under Unesco sponsorship, will soon make available reports from the Benelux countries, France, India, Italy, Japan, the Scandinavian countries, Switzerland, the United Kingdom, and the United States. The committee has begun a compilation of regulations pertaining to animal import and export. ICLA plans a symposium on "Living Animal Material for Biological Research" to be held in September, near Paris.

* * *

A new standard is available for devices that convert sounds from electric to acoustic systems. It is the *American Standard Z24.24-1957, Procedures for Calibration of Electroacoustic Transducers, Particularly for Use in Water,* just published by the American Standards Association, 70 E. 45 St., New York 17.

* * *

The Atomic Energy Commission has confirmed that for the past several months a comprehensive review of its organization has been in progress. The study was conducted by a small task force headed by Assistant General Manager Harry S. Traynor in collaboration with John G. Adams, attorney and consultant.

* * *

The *Manchester Guardian* has recently pointed out that the word "scientist" did not exist prior to 1840. Writing in volume 1 of the *Philosophy of the Inductive Sciences,* Rev. William Whewell commented, "We need very much a name to describe a cultivator of Sciences in general. I should incline to call him a Scientist." Previously, journal articles described such folk as "men of science."

* * *

Two leading institutions in Seoul, Korea, Chosun Christian University and Severance Union Medical College, have been united under the name of Yonsei University. The new coeducational university, with an enrollment of some 4000 students, begins its existence with two major building programs under way—the rehabilitation program initiated by Chosun Christian and the new medical school and hospital complex that was started by Severance Union. In addition, a recent grant from the China Medical Board of New York, Inc., provides $450,000 toward a building for the teaching of the basic medical sciences in the medical school.

* * *

In the university city of Aleppo, Syria, a Syrian Society for Scholarly and Scientific Research has been founded. Its task is to further all scholarly and scientific research and to report on new discoveries in other parts of the world and draw attention to their value. The president of the society is Mohamed Yahia Haschmi.

Scientists in the News

DETLEV W. BRONK, president of the National Academy of Sciences and of the Rockefeller Institute for Medical Research, and LINUS C. PAULING, Nobel laureate and professor of chemistry at California Institute of Technology, have been awarded membership in the Soviet Academy of Sciences. They were among the first group of non-Soviet citizens to be honored in this way. In the past, the U.S.S.R. has recognized outstanding work by foreign scientists through "peace prizes," awards that usually took political factors into consideration.

The Soviet Academy elected 26 new Russian academicians and 55 corresponding members. The appointments raised total membership to 167 academicians and 361 corresponding members.

The new foreign members included two Canadians, EDGAR STACY and WILDER PENFIELD, and three Britains: Sir CYRIL HINSHELWOOD, president of the Royal Society; JOHN D. BERNAL, physicist at Cambridge University; and CECIL F. POWELL, physicist at the University of Bristol. Other scientists elected included representatives of France, Italy, the United Arab Republic, Sweden, East Germany, the People's Republic of China, Poland, Yugoslavia, Japan, and Belgium.

The Department of State has announced the appointment of LARKIN H. FARINHOLT as deputy science adviser. Since 1947 he has been a member of the chemistry faculty of Columbia University. He has left his post there as professor of chemistry and director of chemical laboratories to take up his new duties in Washington.

The 11th World Health Assembly, which met in Minneapolis in May and early June, elected LEROY E. BURNEY, the Surgeon General of the United States, as president of the assembly. He succeeded SABIN HASSAN AL-WAHBI of Iraq. Vice presidents elected by the World Health Organization were J. ANOUTI, Director General, Ministry of Public Health, Lebanon; TRAN VY, Health Minister, Vietnam; and A. SAUTER, Director of Public Health, Switzerland.

N. N. PESONEN, Director General of the State Medical Board of Finland, was chosen chairman of the committee on programs and budget, while S. KHANACHET, member of the Saudi Arabian Legation at Bonn, was selected to head the committee on administration, finance, and legal matters.

Burney, as president of the assembly, presented the Leon Bernard Foundation Prize to THOMAS PARRAN, former U.S. Surgeon General. The prize was established by the League of Nations in recognition of outstanding achievements in the field of social medicine. Parran was chosen because of his contributions to the development of U.S. public health services, and particularly for his part in expanding national control programs against venereal diseases, tuberculosis and cancer, and for providing assistance to states establishing large-scale programs of grants for hospital construction.

The following members of the Harvard Faculty of Public Health retired on 1 July: JOHN E. GORDON became professor of preventive medicine and epidemiology, emeritus; HAROLD C. STUART became professor of maternal and child health, emeritus; and FRANZ GOLDMAN became associate professor of medical care, emeritus.

CARLOS L. GONZALEZ, Minister of Health of Venezuela, has been appointed assistant director of the Pan American Sanitary Bureau, Regional Office of the World Health Organization in Washington, D.C.

CHAUNCEY STARR, vice president of North American Aviation, Inc., and general manager of its Atomics International Division in Canoga Park, Calif., has been elected president of the American Nuclear Society.

Major General ALVIN R. LUEDECKE, U.S. Air Force, has been appointed general manager of the Atomic Energy Commission. He succeeds K. E. FIELDS, who resigned on 1 July. Luedecke, at present commander, Joint Task Force Seven, will assume his new responsibilities after the conclusion of the present series of weapon tests in the Pacific. He will retire from active duty in the Air Force at that time.

In addition, R. W. COOK, deputy general manager of the AEC, has submitted his resignation, effective not later than the adjournment of this session of Congress. Cook will be employed by the executive office of the American Machine and Foundry Company, New York, N.Y.

WERNHER VON BRAUN, director of the Development Operations Division of the Army Ballistic Missile Agency at Huntsville, Ala., has received the Robert H. Goddard Memorial Trophy for outstanding achievement in the field of missiles. He was cited for directing the Jupiter program, which produced the nation's first intermediate range ballistic missile and the first United States earth satellite, the Explorer.

LUDWIG FLECK, formerly head of the department of microbiology and immunology, Mother and Child Institute, Warsaw, and a member of the Polish Academy of Science, has recently joined the Israel Institute for Biological Research, Ness–Ziona, Israel.

MAURICE LEBOSQUET, a Public Health Service commissioned officer since 1936, has been assigned to the International Cooperation Administration as chief sanitary engineer of the Technical Cooperation Mission to India. LeBosquet, from headquarters in New Delhi, will provide assistance in dealing with environmental sanitation problems, particularly those relating to water supply and water pollution control. He left for India on 14 June.

CHARLES HEIDELBERGER and DAVID PRESSMAN have been named the first recipients of the $500 Bertha Goldblatt Teplitz Award, which is presented by the Ann Langer Cancer Research Foundation of Chicago "for meritorious investigation by a scientist under 45." Heidelberger, associate professor of oncology at the McArdle Memorial Laboratory for Cancer Research, received the award for his basic research on 5-fluorouracil, which is important in cancer chemotherapy. Pressman, director of research at the Roswell Park Memorial Institute of the New York state department of health, was honored for his work on techniques for labeling antibodies with radioisotopes.

The Presidential Medal of Freedom has been awarded posthumously to MARK M. MILLS, nuclear physicist, for "exceptionally meritorious service in contributing to the security of the United States of America and the welfare of the human race." Mills, who was deputy director of the University of California Radiation Laboratory, Livermore Branch, was killed in April in a helicopter crash in the area of Eniwetok Atoll while serving as technical director of a nuclear weapon test.

FREDERIC S. ORCUTT, professor of bacteriology at Virginia Polytechnic Institute, has been named acting head of the institute's biology department. He succeeds I. D. WILSON, who has retired after serving for nearly 35 years as head of the department. Wilson retired before the end of the academic year in order to accept a 2-year appointment as an educational adviser in India.

RICHARD A. NOYES, associate professor of chemistry at Columbia University, has been appointed professor of chemistry at the University of Oregon, Eugene. In addition, JOHN SCHELLMAN has been appointed associate professor of chemistry at Oregon. At present he is assistant professor of chemistry at the University of Minnesota.

J. E. P. L. VIGOREUX, senior principal scientific officer, and G. H. RAYNER, principal scientific officer, both of the National Physical Laboratory, Teddington, Middlesex, England, will be in the United States 11–22 August. They will attend the conference on electronic standards and measurements at the National Bureau of Standards Boulder Laboratories 13–15 August, and will also visit the NBS in Washington.

In addition, A. FRANKS, also a senior scientific officer at Teddington, will be in this country 7 September–8 October to attend a conference on small angle scattering in metals at the Midwest Research Institute, Kansas City, Mo., 23–25 September. He will visit Washington; New Brunswick, N.J.; New York; Boston; Buffalo; Milwaukee; Chicago; Rolla, Mo.; Kansas City; Stanford, Calif.; and Redlands, Calif.

HAROUN MAHROUS, associate professor of electrical engineering at the University of Illinois, has been appointed chairman of the electrical engineering department of the Pratt Institute Engineering School.

THEODORE H. INGALLS, formerly associate professor of epidemiology at the Harvard University School of Public Health, has joined the University of Pennsylvania School of Medicine as

professor of preventive medicine and epidemiology. Ingalls will direct a Kellogg Foundation research project aimed at evaluation of periodic health examinations for the early detection and prevention of chronic diseases.

In addition, he will develop projects for evaluating radiation hazards, and for the control of congenital defects. As part of this program, a registry of inherited and acquired abnormalities will be instituted at the new West Philadelphia Health Center. A clinical registry of congenital anomalies, or defects, will also be maintained for counseling purposes.

ROBERT B. HOWARD has succeeded HAROLD S. DIEHL, as dean of the University of Minnesota's College of Medical Sciences. Diehl has retired after holding the deanship since 1935. He has accepted an appointment with the American Cancer Society as senior vice president for research and medical affairs and deputy executive vice president.

CHARLES W. BUGGS, professor of microbiology in the Howard University College of Medicine, became head of the department of microbiology on 1 July.

The American Society for Engineering Education has honored four engineering educators for their outstanding contributions in teaching and research.

LINTON E. GRINTER, dean of the Graduate School and director of research at the University of Florida, received the Lammé Medal for distinguished service in engineering education.

WILLIS W. HARMAN, professor of electrical engineering at Stanford University, received the $1000 George Westinghouse Prize, which is given to a young teacher of outstanding ability.

HUNTER ROUSE, director of the Institute of Hydraulic Research at the State University of Iowa, received the Vincent Bendix Award for outstanding research contributions.

CEDOMIR M. SLIEPCEVICH, head of the department of chemical engineering and associate dean of the College of Engineering at the University of Oklahoma, received the $1000 Curtis W. McGraw Award, which is given to an outstanding young college research worker.

The Scientific Committee of the National Neurological Research Foundation has announced that three men have been named National Neurological Research Foundation scientists and will receive awards of from $10,000 to $12,000 a year for 5 years. These unusual awards mark the first time (except in Government) that basic research has been united in the following areas: multiple sclerosis, Parkinson's syndrome, amyotrophic lateral sclerosis, muscular dystrophy, cerebral palsy, and epilepsy. The award recipients are: MICHAEL V. L. BENNETT, research associate, department of neurology, College of Physicians and Surgeons, Columbia University; BYRON H. WAKSMAN, assistant professor of bacteriology and immunology, Harvard Medical School, and associate bacteriologist, Neurology Service, Massachusetts General Hospital; and DIXON M. WOODBURY, associate research professor of pharmacology, University of Utah College of Medicine.

The National Neurological Research Foundation, founded in 1956, is a nonendowed, voluntary, tax-exempt organization with headquarters at 3255 N St., NW, Washington, D.C.

ELI LILLY, chairman of the board of directors of Eli Lilly and Company, has been selected by the past presidents of the American Pharmaceutical Association to become the recipient of the 1958 award of the Remington Honor Medal. He will be the 35th recipient of this medal, which was established by the New York Branch of the American Pharmaceutical Association in 1918, to be presented annually to the individual who has done most for American pharmacy in the previous year, or whose continuing contributions to the advancement of the profession over a period of years have been most outstanding.

NOBUHIKO SAITO and TSUNENOBU YAMAMOTO of Japan will be visiting professors of chemistry at the University of Oregon, Eugene, during 1958–59. Saito is an assistant professor in the department of applied physics, Waseda University. Yamamoto is professor of chemistry at the University of Kyoto. Both are working in solid-state physics and theoretical chemistry.

JOSEPHINE M. GLEASON has retired from her post as professor of psychology at Vassar College.

TROY L. PEWE, staff geologist, Alaskan Geology Branch, U.S. Geological Survey, and associate professor of geology at the University of Alaska, recently returned to College, Alaska, after spending a season in Antarctica. Péwé was in charge of a glacial geology party of the U.S. National Committee of the International Geophysical Year. He served in the McMurdo Sound area, where observations were made with regard to Quaternary glacial chronology, permafrost, and polygonal ground.

H. LUBINSKI of Jewish General Hospital, Montreal, Canada, has been named emeritus professor of bacteriology by the government of the Federated Republic of West Germany.

ROBERT L. STUBBINGS, research associate professor of chemistry at Lehigh University, is this year's recipient of the Alsop Award of the American Leather Chemists Association. He was selected for "making science and research a useful tool for the tanner."

Recent Deaths

KURT ALDER, Cologne, Germany; 55; former director of research with I. G. Farben, Cologne, Germany; named professor at Kiel University in 1934 and director of the Chemical Institute at the University of Cologne in 1940; one of the 18 Nobel Prize winners who in 1955 signed a declaration warning against a nuclear catastrophe; 20 June.

HALBERT P. GILLETTE, Los Angeles, Calif.; 88; engineer and hydrologist; founder and president of the Gillette Publishing Company of Chicago; performed research on rain and earthquake cycles; 18 June.

SETH G. HESS, New York, N.Y.; 65; director and chief engineer of the Interstate Sanitation Commission; taught at the graduate school of New York University; 18 June.

ALMA E. HILLER, Lynbrook, N.Y.; 66; associate professor of biological chemistry at the Medical College of the University of Illinois until her retirement in 1957; biochemist at the hospital of the Rockefeller Institute for Medical Research in New York 1918–48; author of a textbook, *Practical Clinical Chemisty*; 19 June.

JAROSLAV H. HULKA, Queens, N.Y.; 64; director of the opthalmology department of St. John's Hospital, Long Island City; associate surgeon at the Manhattan Eye, Ear and Throat Hospital; established in 1947 an ophthalmology clinic in Czechoslovakia under the American relief program; author of *Statistics of Tuberculosis in Czechoslovakia* and *Medicine in America*; 18 June.

UMPHREY LEE, Dallas, Tex.; 65; chancellor emeritus of the Southern Methodist University and president from 1938 to 1954; 23 June.

ROBERT M. LEWIS, New Haven, Conn.; 72; associate clinical professor of obstetrics and gynecology at the Yale University School of Medicine, from 1925 until his retirement in 1954; 20 June.

JOHN A. MacDONALD, Interlaken, N.Y.; 81; emeritus professor of clinical Medicine at the Indiana University School of Medicine; 18 June.

J. LOUIS RANSOHOFF, Cincinnati, Ohio; 78; professor of clinical surgery in the College of Medicine at the University of Cincinnati and director of surgery at the Jewish Hospital in Cincinnati; practiced surgery for more than a half-century; 17 June.

Book Reviews

Ancient Man in North America. H. M. Wormington. Denver Museum of Natural History, Denver, Colo., ed. 4, 1957. xviii + 322 pp. Illus. Cloth, $5.25; paper, $3.65.

Eighteen years ago the Denver Museum of Natural History and H. Marie Wormington initiated publication of a series of books called the "Popular Series"; this service has become increasingly useful. The book reviewed here, one of the series, is an unusually complete encyclopedia of the archeology and physical anthropology of ancient man in North America. Every known early camp site and group of artifacts has been described. Such descriptions are often brief, but ample reference is provided for those who are in search of detail. The account is designed to inform the interested nonprofessional reader, but it will be of great value and use to archeologists and other scholars as well.

Introductory chapters that discuss the glacial regimen and climatic cycles in relation to anthropogeography during Pleistocene and Recent geologic time, and also methods of dating, are followed by descriptions of the ancient stone industries. This culture is here divided into three major traditions which, as far as I am aware, are newly proposed. They would be more easily comprehended if they had been discussed a little more thoroughly. Under "Paleoeastern Tradition" are discussed the Folsom Complex —a large number of single sites and a few groups of sites producing culture complexes, all including fluted arrow or dart points. The Folsom Complex is seen to have a distribution somewhat restricted to the Central Plains. On the other hand, points comparable to the Clovis fluted points are distributed from Massachusetts to New Mexico and beyond. There is a stronge reluctance on the part of the author to consider specifically the possible implications of such a distribution of an arrow-point type and of the association of arrow points with widely varying inventories of other tools at a time which could be well before 10,000 B.C. Also included in this Paleoeastern tradition are a number of camp sites and types of dart points which are somewhat later in time. Located largely in the Southwest and in the Plains are Plainview-type points, Angostura, Scottsbluff, and Eden points, and a number of others of equal significance. The description is carried into the Middle West where, at sites such as Graham Cave in Missouri, slightly different shaped points appear to belong to a comparable stage.

The Paleowestern tradition includes industries which have also been called the "desert cultures." Here we see a wide variety of dart points combined with many kinds of scrapers, heavy core implements, grinding tools, and the like which were used by people who subsisted on small mammals and on wild seeds and berries which they harvested. Although some of these industries were contemporaneous with the early Paleoeastern, the people did not hunt the mammoth and now extinct forms of bison as did their eastern counterparts. The third tradition, Paleonorthern, includes material from Alaska, the Yukon, and the Northwest Territories which appears to be a mixture of several stone technologies, some having probable antecedents in the Old World, some being distantly related to technological developments to the south, and the remainder appearing (probably because of lack of knowledge) to be isolated. The antiquity and, in fact, the relative sequence of most of these northern cultures is an open question, and the several hypotheses all have their adherents. As yet the Paleonorthern tradition throws but little light on the earlier migrations from the Old World to the New. The author briefly reviews the various problems and hypotheses.

The preceding synopsis barely outlines the wealth of information presented, for it omits a number of significant, isolated and hardly classifiable discoveries. Among other things, this book gives evidence of the great advance in archeological knowledge which has taken place during the past decade or two. Where 80 pages were sufficient in the 1939 edition, here some 309 pages of description have been required to summarize adequately data from the author's observations and from the references (nearly 600 in this edition, given in an excellent bibliography). More than half of the latter have appeared during the last decade. This increase in the size of the volume is due to the need for description of recent discoveries. Important though this may be, it appears at times to have limited the value of the presentation. Great emphasis has been placed on the dart points, which sometimes are considered to be the only feature from a camp site which provides a basis for classification. The lack of attention to scrapers, core implements, and other tools can be somewhat misleading and will become more so as investigation brings to light more complete inventories of the cultural units. Additional illustrations and some description of tools other than the points would have broadened the base of this book enormously.

I also feel that the book comes close to being a catalog of special things partially or wholly extracted from their surroundings. This robs the picture of ancient cultures that is presented of a certain amount of depth. Furthermore, this characteristic of the book is not truly representative of the status of archeological investigation of ancient man in America. Historical-developmental hypotheses have been postulated by a number of archeologists who are concerned with the evolution of American cultures. These hypotheses, of course, have been derived from a study of the factual material. Some attention to these contributions would have given the book greater breadth. However, American archeology is presently in a state of rapid growth, and the ideas which are appearing may be unusually transitory. Perhaps the author has been wise to restrict herself to brief, objective description. Taken from this point of view, it would be difficult to see how a more useful compilation could have been made.

FREDERICK JOHNSON
R. S. Peabody Foundation, Andover, Massachusetts

The Invertebrata. A manual for the use of students. L. S. Borradaile and F. A. Potts, with chapters by L. E. S. Eastham and J. T. Saunders. Revised by G. A. Kerkut. Cambridge University Press, New York, 1958. xvii + 795 pp. Illus. $8.50.

It is a rare occurrence in recent times when a new textbook on the subject of invertebrate zoology is published, and therefore the appearance of a revised edition of a highly respected volume, when the revisions are as extensive as they are in this case, is a welcome event indeed. Even a superficial examination of the book reveals that it has taken on a substantially new cast. There are more illustrations, and numerous new ones. With the exception of the rare halftones, all are superior to those of the earlier editions—superior not only because a better grade of paper is used but also because the labels are printed on the

figures rather than in the legends. A good number of simplified diagrams have also been used in this edition. More subtitles have been provided in the text, and this remedies a condition which made earlier editions somewhat unpopular among students. The text treatment is, except for changes in organization, rather similar to that of the earlier editions and seems to have received least attention in the revision. The emphasis is clearly morphological.

The classification used in the organization of the book is essentially that found in the earlier editions, with a few exceptions. One is glad to find the Endoprocta and Ectoprocta separated into two phyla and the Graptolita now treated with the protochordates. The phyla Priapulida and Kinorhynchia, omitted from earlier editions, are now included, albeit very briefly. The sections on the Nemertea, Nematoda, Araneida, and Onychophora have been slightly expanded. The minor phyla, however, still continue to be treated very superficially; more than 50 percent of the text is devoted to Protozoa and Arthropoda. With the increasing tendency to make protozoa and insects the subjects of special courses and to consider them apart from the remainder of the invertebrates, this emphasis is not always desirable.

A new chapter, entitled "Literature," has been added. This is an interesting introduction for the student to further sources of information on all phases of invertebrate zoology.

In summary, although this book is on a subject so extensive in scope that the choice of content has, of necessity, been somewhat arbitrary and hence will not please everyone, the character and certainly the general quality of the coverage make this volume one of the best general undergraduate textbooks available.

F. A. Brown, Jr.
Department of Biological Sciences, Northwestern University

The Problem of Scientific and Technical Manpower in Western Europe, Canada and the United States. 2nd report. Organisation for European Economic Co-operation, Paris, 1958. 221 pp. $2.

The Organisation for European Economic Co-operation has shown a steadily expanding interest in studying the scientific and engineering manpower trends and the problems of education and utilization of technological manpower in the OEEC countries. This volume is OEEC's second statistical report on supply and demand in the sciences and applied sciences. Also included is employment information and information on the numbers graduating from universities and other institutions. The information differs somewhat from country to country due to differences in the detail and completeness of available records. Comparisons between nations must be interpreted in light of differences in terminology and educational systems. Nevertheless, the report is a valuable source of scientific and technical manpower information for the member countries—Austria, Belgium, Denmark, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, the Netherlands, Norway, Portugal, Sweden, Switzerland, Turkey, and the United Kingdom—and for Canada and the United States, which are not member countries but which cooperate closely with OEEC.

Dael Wolfle
American Association for the Advancement of Science

Treatise on Marine Ecology and Paleoecology. vol. 1. *Ecology.* Joel Hedgpeth, Ed. vol. 2. *Paleoecology.* Harry S. Ladd, Ed. Memoir 67. Geological Society of America, New York, 1957. vol. 1, viii + 1296 pp., $12.50; vol. 2, x + 1077 pp. $10.

The breadth of the world's seas and their deepest dimensions scarcely exceed the scope of these outstanding reference volumes. Each is a monument to its editor and to the scores of specialists who contributed so fully. Each volume consists of a series of chapters with individual bibliographies, summarizing present knowledge on representative topics, followed by still different annotated bibliographies and an index.

Of the 29 chapters in volume 1, about a third are contributions from the Scripps Institution of Oceanography, another third from European authorities in Denmark, Finland, Germany, the Netherlands, the U.S.S.R. and the United Kingdom. After classifying marine environments and considering methods used to obtain ecological data from the sea, the specialists have analyzed modern understanding of physical and chemical factors, marine biogeography and bottom characteristics, and the living communities of major habitats as far as high-tide line on rocky shores and sandy beaches and into estuaries, with special consideration given the Baltic, Black, Caspian, and Aral seas. A combination of case-history method and informed speculation features the final chapters on lunar periodicity, fluctuations in littoral populations, and the etiology of mass mortality in the sea. The annotated bibliographies (215 pp.), each by a specialist, group ecological publications by taxonomic groups of animals and plants.

Of the 24 chapters in volume 2, about a third are by members of the U.S. Geological Survey; all are from this country. An initial six chapters give general consideration to evidence from the fossil record about ecological conditions of the past. The next 15 chapters go carefully into selected North American samples—the paleoecological inferences derived from individual formations—representing the full time scale from the Precambrian to the marine Pleistocene. By way of comparison, two chapters are given over to analysis of modern situations favorable to fossilization, one in bays of the central Texas coast, the other in a tidal flat in Maine. G. Evelyn Hutchinson has attempted to peer into the future of marine paleoecology in a final chapter. The annotated bibliographies (342 pp.) are again on a taxonomic base, but often broken down into separate treatments by geological horizon. As in volume 1, the annotations are at least as valuable as the references themselves, and a conscientious attempt has been made to include pertinent material in all languages (including Russian).

These volumes will probably wear out from repeated use before they grow too out-of-date. All scientists concerned with the sea and the fossil record of its past will need to refer constantly to the *Treatise* and should bless the several organizations which have made the publication in present form a possibility.

Lorus J. Milne
Margery Milne
Department of Zoology, University of New Hampshire

Figurets. More fun with figures. J. A. H. Hunter. Oxford University Press, New York, 1958. xi + 116 pp. Illus. $3.50.

This book is not a "survey of mathematics for the layman"; in fact, it makes no pretense of containing much serious mathematics. In the preface, the author calls the book a "selection of teasers . . . meant for people . . . who enjoy figures without being too serious about them." Readers familiar with his earlier volume, *Fun with Figures,* will know what to expect.

The author is more conscientious than some in that when he says his material is within the grasp of the nonmathematician he really means it. The book is a collection of 150 separate short problems presented entertainingly and in many disguises. Nearly all of them can be solved by arithmetic or algebra, but many are by no means easy. Solutions are given (in the back); and as a further (perhaps too kindly) assist to the solver, most of them are classified by code letter in the table of contents so that the general method of solution can be anticipated.

One finds the problems somewhat lacking in variety, but that may be unavoidable within the prescribed scope. Possibly a wider choice from the field of geometry might have provided a dash of something different with which to flavor the algebraic diet.

Although the book is in no sense a textbook, it could well be used by mathematics clubs or for outside reading in connection with high-school mathematics courses. In addition to illustrating many applications of algebra, the book could introduce a student to indeterminate and Diophantine equations, which are often slighted in standard courses. It also gives a glimpse of the fact that many problems cannot be solved without considerable trial and error. If algebra students are unaware of this, it is high time they were told; mathematics is like that!

C. STANLEY OGILVY
Department of Mathematics, Hamilton College

The Handbook of Feedstuffs. Production, formulation, medication. Rudolph Seiden and W. H. Pfander. Springer, New York, 1957. xii + 591 pp. $8.

Animal feeding has become an ever more complicated and competitive business that requires a sound foundation in agronomy, animal husbandry, biochemistry, botany, nutrition, pharmacology, physiology, and economics. It is obvious that no agricultural agent, farmer, feeder, or feedstuff manufacturer can have the up-to-date knowledge in all these fields of basic and applied science necessary for taking advantage of recent advances and discoveries; and even the scientific worker specializing in any one field related to animal feeding needs to have good background information about the present status of the other fields. All such readers will welcome this first encyclopedic collection of facts and figures about feedstuffs, written by an eminent agricultural chemist, who is a consultant on veterinary pharmaceuticals, and by an outstanding animal nutritionist, who is professor of animal husbandry at the University of Missouri.

The *Handbook* lists all feeds produced on ranches and farms or in factories, data on consumption by various kinds of farm animals, and the ratios applied, and discusses the economic significance of these feeds. Since about 25 percent of manufactured feedstuffs contain natural or synthetic supplements, drugs, and growth stimulants, the many substances that recently have come into use as feedstuff additives, such as antibiotics, sulfonamides, arsenicals, vitamins, hormones, and amino acids, are described and discussed from a physiological and nutritional viewpoint. Although the work is based upon the investigations of hundreds of experts, the authors have succeeded in presenting even involved scientific matters in simple and understandable language, thus making the information accessible also to the farmer and student of agriculture, who, like the other users of the work, will find its comprehensiveness and the alphabetical arrangement of its extensive subject matter most convenient.

FRANCIS JOSEPH WEISS
Arlington, Virginia

New Books

Mental Deficiency. In relation to problems of genesis, social and occupational consequences, utilization, control and prevention. J. E. Wallace Wallin. Journal of Clinical Psychology, Brandon, Vt., 1956. 200 pp. $5.

Georgia Birds. Thomas D. Burleigh. University of Oklahoma Press, Norman, 1958. 775 pp. $12.50.

Clinical Enzymology. Gustav J. Martin, Ed. Little, Brown, Boston; Churchill, London, 1958. 248 pp. $6.

Lumber. Nelson Courtlandt Brown and James Samuel Bethel. Wiley, New York; Chapman & Hall, London, ed. 2, 1958. 393 pp. $9.

Annual Review of Medicine. vol. 9. David A. Rytand and William P. Creger, Eds. Annual Reviews, Stanford, Calif., 1958. 530 pp. $7.

Protides in the Biological Fluids. Proceedings of the fifth colloquium, Bruges, Belgium, 1957. H. Peeters, Ed. Elsevier, Amsterdam, 1958. 260 pp. $8.50.

A Short Introduction to Archaeology. V. G. Childe. Macmillan, New York, 1958. 142 pp. $2.50.

A Sourcebook for the Biological Sciences. Evelyn Morholt, Paul F. Brandwein, Alexander Joseph. Harcourt, Brace, New York, 1958. 521 pp.

Nerves Explained. A straightforward guide to nervous illnesses. Richard Asher. Thomas, Springfield, Ill., 1958. 157 pp. $2.75.

Studies in the Mathematical Theory of Inventory and Production. Kenneth J. Arrow, Samuel Karlin, Herbert Scarf; contributions by Martin J. Beckmann, John Gessford, Richard F. Muth. Stanford Univ. Press, Stanford, Calif., 1958. 350 pp. $8.75.

Advances in Chemical Engineering. vol. II. Thomas B. Drew and John W. Hoopes, Jr. Academic Press, New York, 1958. 348 pp. $9.50.

Phenolic Resin Chemistry. N. J. L. Megson. Academic Press, New York; Butterworths, London, 1958. 230 pp. $10.80.

Physical Optics. R. A. Houstoun. Interscience, New York, 1958. 306 pp. $6.25.

Professional Ethics and Civic Morals. Emile Durkheim. Translated by Cornelia Brookfield. Free Press, Glencoe, Ill., 1958. 272 pp. $5.

The City. Max Weber. Translated and edited by Don Martindale and Gertrud Neuwirth. Free Press, Glencoe, Ill., 1958. 242 pp. $4.

La Souche du BCG. Monographie de l'Institut de Microbiologie et d'Hygiène de l'Université de Montréal (en collaboration avec le Département de Bactériologie de la Faculté de Médecine et avec l'École d'Hygiène). A. Frappier and M. Panisset. Institut de Microbiologie et d'Hygiène de l'Université de Montréal, Montreal, Canada, 1957. 120 pp.

Textbook of Dendrology. Covering the important forest trees of the United States and Canada. William M. Harlow and Ellwood S. Harrar. McGraw-Hill, New York, ed. 4, 1958. 572 pp. $8.75.

Applied Physiology of the Eye. H. Willoughby Lyle and T. Keith Lyle. Bailliere, Tindall and Cox, London, 1958 (order from Williams & Wilkins, Baltimore). 349 pp. $9.

Traité de Zoologie. vol. XIII, *Agnathes et Poissons.* Anatomie, ethologie, systematique. Pierre P. Grassé, Ed. Masson, Paris, 1958. 924 pp. Paper, F. 12,000; cloth, F. 13,000.

Traité de Paleontologie. L'origine des mammifères et les aspects fondamentaux de leur evolution. vol. VI, *Mammifères, Evolution.* Jean Piveteau, Ed. Masson, Paris, 1958. 962 pp. Paper, F. 15,500; cloth, F. 16,500.

Matière et Antimatière. Maurice Duquesne. Presses Universitaires de France, Paris, 1958. 126 pp.

The Teaching of Geography. Zoe A. Thralls. Appleton-Century-Crofts, New York, 1958. 347 pp. $3.75.

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Reports

Drug Synergism (Potentiation) in Pain Relief in Man: Papaverine and Morphine

For the clinical evaluation of analgesics two general methods are in use: (i) One group receiving one drug is compared with a different group medicated with another drug. (ii) The patient is used as his own control, receiving both drugs on different occasions. Comments on these methods have been made by Beecher (*1*). He pointed out that method i suffers from inconsistency among patients and requires a larger series, whereas in method ii, which is employed in this laboratory, the possibility of drug interaction is present.

In recent experiments in this laboratory, papaverine was tested as an antipruritic and was compared with morphine in experimental and pathologic pruritus in man. Since both morphine and papaverine appeared to relieve pathological pruritus, and since there is reason to believe that itch and pain are mediated by the same apparatus (*2*), papaverine was compared with morphine in pathological pain. Here, unexpectedly, an example of drug interaction was observed.

In a "double-blind" experiment 69 patients with abdominal, thoracic, and major orthopedic operations were studied postoperatively to determine relief of steady wound pain, according to methods previously described (*1*). The pain was rated as "severe" or "moderate" before medication was given. Forty-five patients received morphine, 10 mg, alternating with papaverine, 50 mg, and 24 patients received morphine, 10 mg, alternating with papaverine, 100 mg. These weights refer to the salts and were contained in 1 ml of solution. The drugs were injected subcutaneously, per 70 kg of body weight. After a drug was given, the patients were visited by technicians at 45, 90, 150, 210, 270, and 330 minutes after medication.

The pain was recorded as "unchanged," "less than half gone," "more than half gone," or "disappeared." The relief reported by the patient was then rated as 0, 1, 2, and 3, respectively. Only "paired" data were evaluated—that is, data for doses of morphine and papaverine given to the same patient for the same degree of pain. The effects of the drugs on "moderate pain" and "severe pain" were examined separately.

The data were analyzed as previously described by Gravenstein and Beecher (*3*). When the pain level is controlled and correlated data are used, papaverine, 50 mg, and 100 mg, is consistently less effective than morphine, 10 mg. An analysis of variance of these data shows a significant difference in pain relief between morphine and papaverine at all times with either dose. The relief with papaverine in the 50-mg dose is that expected from a placebo (25 percent versus 30 percent). Papaverine, 100 mg, relieved 14 percent of the patients in pain. The difference in analgesic power between papaverine, 100 mg, and morphine, 10 mg, is consistently greater than the difference between papaverine, 50 mg, and morphine, 10 mg. This curious "antianalgesic" effect of the larger dose of papaverine is similar to the effect of the dextrorotatory form of iso-methadone, on which Denton and Beecher commented (*4*).

Data from all patients who received morphine or papaverine as their very first and second postoperative medication for the given pain level are presented in Table 1. In this group morphine, 10 mg, was found to be more effective when given as the second drug following papaverine than when given as the first drug—that is, preceding papaverine. For the statistical analysis of this difference, the only data used were those which were obtained from 18 patients medicated for one pain level, moderate pain. Pain relief was significantly better for all checks 45, 90, and 150 minutes after medication ($p < 0.01$ in all three checks) when morphine was given as the second drug postoperatively, following papaverine, as compared with the identical dose of morphine given as the first postoperative medication. In the group of patients with severe pain the numbers are too small for statistical analysis; however, the results corroborate the findings for moderate pain.

Papaverine has no analgesic power. The significance of this fact in view of its antipruritic effectiveness is interesting and is discussed elsewhere (*5*). Great interest attaches to the finding that in this study where the patients serve as their own control, morphine given as the very first drug postoperatively was much less effective than the identical dose of morphine given after papaverine. This cannot be explained as an effect of waning postoperative pain, since the pain level was controlled and since it has been shown (*3*) that the pain levels identified by the patients are sufficiently reliable as measurements of intensity of pain. It is conceivable that the very first pain report by a patient is different from the second. This possibility can be examined in the data of Gravenstein and Beecher (*3*). These data therefore were reevaluated, and the pain relief afforded by the first dose of morphine was compared with that afforded by a second and identical dose in the same patient given for the same degree of pain. In 24 patients there is no difference in pain relief between doses one and two. These data are presented in Table 2. The conclusion that less pain relief is obtained from morphine not preceded by papaverine therefore gains significance.

The question can be raised whether this is due to some specific effect of papaverine or whether the same phenomenon could be observed with other drugs. Data from a study of identical design as the papaverine experiment just described, in which dihydrocodeine, 30 mg, was compared with morphine, 5 mg, and

Table 1. Mean pain relief scores for 18 patients with moderate pain. Patients were given morphine, 10 mg, preceding or following papaverine, 50 mg, as the first postoperative medication.

Injection	Score		
	45 min	90 min	150 min
Morphine following papaverine	2.44	2.67	2.56
Morphine preceding papaverine	1.11	1.67	1.67
Difference	+1.33	+1.00	+0.89

All technical papers are published in this section. Manuscripts should be typed double-spaced and be submitted in duplicate. In length, they should be limited to the equivalent of 1200 words; this includes the space occupied by illustrative or tabular material, references and notes, and the author(s)' name(s) and affiliation(s). Illustrative material should be limited to one table *or* one figure. All explanatory notes, including acknowledgments and authorization for publication, and literature references are to be numbered consecutively, keyed into the text proper, and placed at the end of the article under the heading "References and Notes." For fuller details see "Suggestions to Contributors" in *Science* 125, 16 (4 Jan. 1957).

Table 2. Mean pain relief scores for 24 patients given two 10-mg doses of morphine.

Dose	Severe pain		Moderate pain	
	45 min	90 min	45 min	90 min
1	1.93	2.07	2.44	2.44
2	1.93	2.27	2.22	2.44
Difference	0.00	+0.20	−0.22	0.00

again with morphine, 10 mg, suggested that morphine following dihydrocodeine would be more effective than when given alone. Data on these studies are limited to few patients, not justifying statistical analysis, and can serve only as suggestive support.

So far as we have found, the material presented here is the first occasion where synergism in the relief of pathological pain in man has been clearly demonstrated with analgesic drugs. Attention must be called, however, to the related work of Macht (*6*). Macht worked on himself and two colleagues with experimental pain produced by the Martin method. He failed to use essential controls and arrived at the erroneous conclusion that papaverine is a powerful analgesic. He did report, among other things, that the analgesic effect of morphine is increased when it is combined with narcotine, a drug chemically related to papaverine.

In animals (*7*), evidence suggesting a synergism between morphine and drugs pharmacologically related to papaverine has been published. However, the literature contains no report on the interaction between morphine and papaverine in pathological pain, and no suggestion about the possible mode of interaction in this situation. Veldstra (*8*) has discussed synergism in general and has attempted to formulate possible explanations.

On the basis of our data, interaction among drugs in the experimental situation described does occur. No clue about the nature of this interaction is available.

In every experiment which utilizes patients who have received medication before being studied as to their response to an experimental drug, there is the possibility of drug interactions. While investigators using patients with chronic pain have certain advantages, since their experimental design is not limited by waning pain, they are nevertheless confronted by this interaction problem. Patients with chronic pain usually receive pain-relieving opiates and frequently in relatively large dosages while they are not under investigation (*10*). Thus the use of patients with chronic pain creates difficulties in evaluating the "priming" effect of a drug given for the very first time. On the other hand, when patients with postoperative pain are used, the effect of preceding anesthetics cannot be easily evaluated. The same influence can conceivably affect data on respiratory and other side effects when patients with chronic pain are used. It is not suggested that such possible drug interaction completely invalidates the results, but it is emphasized that data obtained under such conditions can be representative only of the conditions under which they were obtained. A complete assessment of the clinical characteristics of a drug therefore is possible only after the drug has been studied under various conditions with different methods (*10*).

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27 February 1958

Current Strontium-90 Level in Diet in United States

Knowledge of the concentration of strontium-90 in the diet permits calculation of the equilibrium level in the human skeleton (*1*). This report (*2*) describes measurements on approximately 100 food samples. Samples of the important calcium (and therefore strontium-90), sources—that is, milk, vegetables, cereals, and tap water—are included.

Each vegetable sample (Table 1) represents 10 packages (about 3 kg) of frozen food, which in turn represent a production run at a food plant. The cereals (Table 2) were 200-g aliquots of a dozen boxes of the most common varieties. Liquid milk samples (Table 3) came mainly from cows that had grazed on unplowed land. Meat, eggs, and fish were omitted because their con-

Table 1. Strontium-90 in common vegetables from various locations, 1956–57.

Sample	Date	SU
Maine		
Peas	8/56	21.3
Western New York State		
Beans, cut green	8/56	20.2
Beans, cut green	9/56	18.4
Beans, cut green	9/56	8.6
Beans, wax	7/57	13.6
Beans, wax	8/57	11.3
Cauliflower	10/56	9.1
Corn	9/56	28.4
Spinach	6/57	1.8
Av.		13.9
Eastern Pennsylvania, New Jersey, Long Island		
Asparagus	6/56	1.2
Asparagus	5/57	1.1
Beans, cut green	12/56	4.6
Beans, cut green	9/56	8.0
Beans, lima	9/56	6.6
Cauliflower	fall/56	8.1
Peas	6/57	10.0
Potatoes, sweet	?/57	13.3
Potatoes, white	?/57	6.1
Squash	fall/56	11.5
Av.		7.3
Eastern Maryland, Delaware		
Asparagus	10/56	1.7
Beans, lima	?/56	2.9
Beans, lima	9/56	8.4
Broccoli	10/56	4.7
Broccoli	10/56	6.7
Broccoli	10/56	8.5
Corn	12/56	3.6
Peas	12/56	1.3
Av.		4.7
Tennessee		
Okra	7/57	18.0
Spinach	?	6.1
Spinach	4/57	1.2
Turnip greens	5/57	21.3
Turnip greens	2/56	7.8
Av.		10.9
Minnesota		
Corn	9/56	1.6
Peas	6/56	5.8
Av.		3.7
Washington, Idaho, Oregon		
Beans, lima	9/55	6.3
Broccoli	9/56	3.7
Corn	8/57	2.1
Peas	6/57	4.8
Peas	7/56	7.8
Peas	6/56	3.0
Potatoes	?/57	8.7
Squash	9/56	3.1
Squash	10/56	3.7
Av.		4.8
California		
Asparagus	4/57	1.8
Beans, lima	5/57	4.6
Beans, lima	9/55	10.0
Beans, lima	9/56	4.3
Broccoli	4/57	4.0
Brussels sprouts	10/56	12.0
Brussels sprouts	9/56	4.3
Brussels sprouts	12/56	2.5
Brussels sprouts	11/56	1.1
Cauliflower	10/56	28.5
Cauliflower	4/57	22.5
Spinach	3/57	13.9
Spinach	3/57	9.1
Spinach	3/57	9.5
Av.		8.5
Av. for all vegetable samples		9.4
Av. for peas, beans, corn, and potatoes		8.7

Table 2. Strontium-90 in common cereals from various locations, 1956–57.

Sample and location	Date	SU
Wheat (New York)	?/56	22.8
Wheat (Washington)	55/56	9.1
Bran (Michigan)	summer/57	8.6
Flour (Illinois)	?/56	6.7
Rice (Unknown)	?/56	4.0
Wheat (Unknown)	?/56	37.5
Oatmeal (Unknown)	?/56	5.7
Av. for all cereals		13.5

tribution to the calcium intake is trivial and because the Sr^{90}/Ca ratio is not expected to exceed that in milk by more than a factor of 2.

The chemical and radiometric procedures have been described elsewhere (*3*). The over-all yield of strontium was monitored with a Sr^{85} tracer. A representative set of six frozen vegetables was prepared according to the directions on the package, and the liquid phase was analyzed separately. No appreciable Sr^{90} is removed in the preparation of the vegetables for human consumption.

The data on U.S. milk (Table 3) include those of the Health and Safety Laboratory of the AEC New York Operations Office (*4*), extrapolated to late 1957 where necessary. The variations in Sr^{90} concentration from one farm to the next are probably related to the available calcium content of the pasture and to the average root depth of its grass. Duplicate milk samples from two nearby farms in Virginia gave 1.9 and 1.9, and 8.1 and 7.1 μμc of Sr^{90} per gram of calcium (hereafter referred to as strontium units, SU), respectively. Variations up to a factor of 2 occur from a single distribution source (Bergen County, N.J.) over a period of a month, reflecting changes in relative quantities of milk from contributing farms in successive batches. Despite these short-time variations, the average monthly value for different parts of the country is quite uniform, giving an average concentration for the country of about 6 SU. In comparison, the average level of Sr^{90} in British milk would be 7 to 8 SU in late 1957, on the basis of an extrapolation of the 1956 data (*5*).

The vegetables and cereals (Tables 1 and 2) are representative of large-acreage production. Variations from one sample to another grown in the same general area probably reflect different soil conditions. No appreciable increase in Sr^{90} from mid-1956 to early 1957 is observable from the data, as is not wholly unexpected, since an increase in Sr^{90} in the total fallout was only about 20 percent during this period.

Geographical differences in the Sr^{90} concentration appear but do not exceed two times the mean. In the diet, however, these differences are averaged out because of the nature of commercial food distribution. Some differences appear among plant types—for example, asparagus is relatively low, but among the major calcium contributors (peas, beans, and cereals), the Sr^{90} level is rather uniform.

The U.S. population obtains 85 percent of its calcium from milk, 4 percent from cereals, and 5 percent from vegetables (*6, 7*). If the average concentration of Sr^{90} in these foods in the United States in late 1957 is assumed to be 6, 15, and 10 SU, respectively, the average diet contains about 6.5 SU. In an extreme case, a vegetarian might have double this value.

Monthly integrated tap-water samples in the New York City area now carry about 0.1 μμc of Sr^{90} per liter. If an average consumption of 1 liter of water and 1 g of calcium from food each day is assumed, the contribution of Sr^{90} from drinking water appears to be negligible. If rain water were consumed, this source would still only account for about 20 percent of the daily Sr^{90} intake.

It is concluded that the Sr^{90} content in the diet of an average U.S. citizen in 1957 was about 6.5 SU, corresponding to an equilibrium base level of 1.6 SU, since the discrimination factor between diet and base appears to be about 4 (*1, 5*). If the diet concentration remains constant for a decade, the equilibrium bone level of 1.6 SU would be approached by young children. New-born children would have about half of this value on account of fetal discrimination, and adults would reach only 20 to 30 percent of the equilibrium level, because of the slow rate of exchange of the calcium in bone.

Table 3. Strontium-90 in milk from various locations, 1956–57. The numbers in parentheses in column 3 give the number of samples.

Location	Date	SU	
New Jersey (Bergen County)	9–10/57	Range	3.0–7.7
		Av.	5.5 (14)
New Jersey (other)	10/57	Av.	5.5 (4)
New York City (retail)*			5.5
New York State (Perry)*			4.5
Mohawk Valley	9–10/57	Av.	6.6 (4)
North Carolina	8/57	Av.	5.3 (4)
North Dakota (powdered)*			10.0
Mississippi (State College, powdered)*	?/56		6.5
Missouri (St. Louis, powdered)*			6.5
Oregon (Portland, powdered)*			7.0
Virginia (Rockingham County)	10/57	Av.	3.8 (4)
Wisconsin (Columbus, powdered)*			5.5
Av. for all 1957 milk			6.1

* Estimated from an analysis reported by Health and Safety Laboratory, New York Operations Office of the AEC (*4*), extrapolated to late 1957.

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17 February 1958

Effect of Zinc on the Determination of Cyanide with Phenolphthalin

Determination of cyanide by the oxidation of phenolphthalin in alkaline solution to phenolphthalein in the presence of a trace of cupric salt and cyanide (*1*) is a method that has been used to determine trace amounts of cyanide in a wide variety of biological and industrial media. The determination is not specific for cyanide but is subject to interference by various oxidizing substances (*2*). Recent work on plating-room wastes in which this method was used has raised the question of the effect of zinc in such solutions. Zinc can form stable cyanide complexes which might cause negative errors.

To ascertain whether or not such errors exist (*3*), a series of known cyanide solutions was made up, and known amounts of zinc were added. This method of determining cyanide consists of adding 2 ml of the unknown to 10 ml of 0.05-percent KOH, followed by 10 ml of indicator solution. The indicator solution consists of 99.5 ml of 1-percent $CuSO_4 \cdot 5H_2O$ plus 0.5 ml of 1-percent phenolphthalin dissolved in 0.67-percent NaOH. This indicator solution is not stable and should be made up fresh every 2 hours. Absorbance is read at 553 mμ, the absorbance peak for phenolphthalein (*4*), 3 minutes after the indicator solution has been added. The calibration curve for cyanide alone is a straight line passing through zero.

One might suppose that, if zinc does complex cyanide with a stability sufficient to interfere with this method of determining cyanide, absorbance would decrease as zinc content increases, falling to zero with the addition of an amount of zinc proportional in some manner to the amount of cyanide present. However, Fig. 1 shows that, as the zinc content is increased, the absorbance increases to a flat maximum, then rapidly falls to zero with addition of a specific amount of zinc which is independent of the amount of cyanide present. The increases in absorbance are neither constant nor proportional to the absorbance in the absence of zinc.

Since the cyanide solutions are basic and the zinc solutions are acidic, the effect of *p*H was briefly investigated. Solutions of NaOH and HCl were made up which matched the zinc and cyanide stock solutions with respect to *p*H. A colored cyanide solution is decolorized by HCl and recolored by NaOH. After the initial addition of HCl, a single drop of base or acid is sufficient to change the color, as one would expect at the end point in an acid-base titration in which phenolphthalein is used as the indicator.

On the other hand, a cyanide solution which has been decolorized with zinc can be recolored by adding cyanide, but more than three times the amount of cyanide originally present is required, and the second color is weaker than the first. This second color can then be discharged with about one-tenth the amount of zinc first required. Subsequent recolorization and decolorization requires an excess of cyanide and only a small amount of zinc.

It is thus apparent that the phenolphthalin method for determining cyanide is subject to interference by zinc. Often when an ion interferes with an analytical method, the method can be adapted as a means of analyzing for that ion. The shape of the curves in Fig. 1 indicates that this cannot be done in the present case. However, by standardizing cyanide in the presence of, say, 6 parts per million of zinc, one would be operating in the flat portions of the curves, and then one could determine cyanide in the presence of zinc without error, as long as the zinc concentration did not vary beyond the limits of 3 to 10 parts per million.

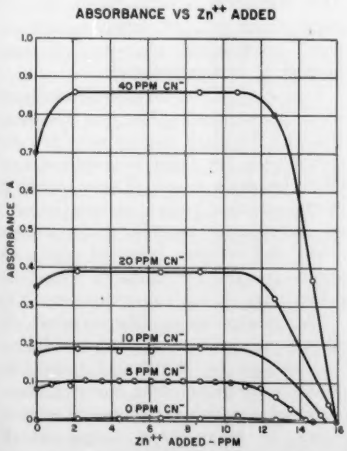

Fig. 1. Absorbance, at 553 mμ, of phenolphthalein due to the presence of cyanide versus amount of zinc added.

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10 February 1958

Reactivation of Cytochrome Oxidase by Lipide

There are reports in the literature which indicate that lipides or lipide-soluble substances may be important for the normal activity of respiratory enzymes. For example, Nason and Lehman (*1*) have investigated the restoration by tocopherol of DPNH- and succinate-cytochrome *c* reductase activity of rat skeletal muscle following isooctane extraction and aging to reduce the activities. Martius and Nitz-Litzow (*2*) have proposed that vitamin K_1 is a necessary component of the DPNH-cytochrome *c* reductase system. They have based their hypothesis on (i) the inhibitory effect on oxidative phosphorylation of dicoumarols and related compounds, (ii) the reduced phosphorylation in mitochondria from the livers of vitamin K-deficient chicks (which is restored by vitamin K_1), and (iii) the identification of a DPN-dependent vitamin K_1 reductase in pig liver mitochondria.

More recently Crane, Hatefi, Lester, and Widmer (*3*) have reported the isolation from beef heart mitochondria of a quinone capable of undergoing reversible oxidation and reduction. This compound, with an absorption maximum at 275 mμ (designated as Q-275), will reactivate the succinoxidase system of heptane-extracted mitochondria, and in the reduced state can be oxidized by ferricytochrome *c* in the presence of the electron-transport particle. Previous reports that implicate a lipide in the cytochrome *c* oxidase portion of the chain include those that demonstrate an inactivating effect of lecithinases (*4*). More recently, Witter, Morrison, and Shepardson (*5*) have found that lysolecithin uncouples phosphorylation from oxidation of ascorbate-cytochrome *c* by the cytochrome oxidase contained in rat liver mitochondria and thus enhances oxygen uptake by about 100 percent.

In the course of attempting to purify the cytochrome oxidase of beef heart mitochondrial fragments (*6*) by extracting with surface active agents, we found that, after treatment of the particles on a cellulose column with deoxycholate (1.9 percent) and with cholate (4.0 percent), the cytochrome oxidase that was finally solubilized with 3 percent deoxycholate (S3) was relatively inactive. The addition of the 4 percent cholate extract (S2), however, reactivated some of the enzyme (Table 1, experiment 1). In another experiment the 1.6-percent deoxycholate extract (S1) proved to be an even better activator (Table 1, experiment 2) of a slightly active 2.5-percent deoxycholate extract (S3).

The activating substance, free of surface-active agents, proved to be heat stable and extractable by butanol but not by ethyl ether or petroleum ether. A number of lipides and lipide-soluble substances were tested for their capacity to activate the enzyme. The following compounds were ineffective: oleic acid, vitamin K_1, cholesterol, DL-α-tocopherol phosphate, choline, and phosphoryl choline. In Table 1, experiment 3, are presented those compounds which proved to be effective activators. There are several possibilities to be considered for the activating effect by these phospholipides:

Table 1. Reactivation of cytochrome oxidase. Cytochrome oxidase activity (*9*) is expressed as the first-order velocity constant.

Fraction	Activity ($\times 10^{-3}$ sec^{-1})
Experiment 1	
S3	0.47
S2	0
S3 + S2	1.34
Experiment 2	
S3	0.69
S1	0.75
S3 + S1	8.54
Experiment 3	
S3	0.93
S3 + animal lecithin (pract.)	4.85
S3 + animal lecithin (purified by chromatography)	1.60
S3 + vegetable lecithin	2.45
S3 + cephalin (impure)	2.80
S3 + dimyristoyl lecithin	2.88

(i) that they are actually involved in electron transport; (ii) that they are facilitating an optimal rearrangement of the reacting components; (iii) that they are removing a surface-active agent which has become attached to the enzyme and has inhibited it. The last possibility is rendered unlikely by the result that removal of deoxycholate with resin from an S3 supernatant does not lead to reactivation.

These results explain a discrepancy observed in our laboratory in 1950. When studying the copper content of cytochrome oxidase (*7*), we noted that there was poor correlation in many instances between the oxygen uptake catalyzed by a fraction and the height of the *alpha*-absorption peak in the reduced state. The ratio, O_2 uptake : 601-mμ absorption, decreased as succeeding fractions were made by extracting heart muscle particles with 1 percent deoxycholate. It may now be suggested that the third and fourth fractions were probably deficient in the lipide or in the lipide-soluble substance being discussed here (*8*).

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Production of Gibberellin-like Substances by Plant Tissue Cultures

One of the most discussed as well as one of the most investigated problems today in the fields of plant physiology and plant agriculture generally is that of the gibberellins and their action on plant growth (*1, 2*). That this group of fungal metabolic products has many very dramatic effects on plants has been amply demonstrated (*2, 3*). How these chemicals act and exactly how valuable they will be to agriculture are two questions which still remain unanswered.

Recently, investigators have reported gibberellin-like activity in extracts from several plants (*4–6*). Most of this type of investigation has been carried out by Phinney and his colleagues. In surveying numerous plants and plant parts, a surprising number of active extracts was found. This led Phinney to suggest that gibberellin-like compounds are widespread and might be universal in their occurrence among flowering plants (*6*). The greatest activity was found in the green seeds, young fruit, and endosperm of several plant species.

The loss of activity as seeds reach maturity, the location of active extracts in stem tips (*7*), and the general activity of immature tissues indicate that immature tissues—rapidly dividing meristematic areas—are the sites of synthesis of these gibberellin-like materials. If this is the case, plant-tissue cultures should be an excellent place to look for such activity. If it is found, this should lend much weight to the hypothesis of universal occurrence in the plant kingdom. Moreover, tissue-culture techniques should lend themselves to investigations of such problems as rate and site of synthesis, nutritional factors affecting synthesis, and control of synthesis.

This is a preliminary report of the results of our survey of plant tissue cultures as sources of gibberellin-like factors.

The tissues used in this study are well-established cultures which have been maintained in our laboratory for several years. The conditions under which they have been grown have been discussed in previous publications (*8*). Extractions were made, in each case, of 20 g (wet weight) of tissue about 4 weeks after its latest subculture. The method of extraction was patterned after that used by Phinney and his co-workers (*5*) and consisted of (i) extraction of diced tissue with acetone-water (1:1) on a shaker for 24 hours; (ii) filtration of the solvent, and (iii) reduction in volume over a steam bath to 5 ml. This 5-ml sample was sprayed with a deVilbiss atomizer on five dwarf pea plants (*9*) (1 ml per plant) which had been planted in sand 1 week previously. Growth of the plants was measured 3, 5, and 7 days after application, and the results were compared with measurements of control plants and of plants sprayed with standard gibberellin solutions.

Table 1. Plant tissue-culture extracts which have gibberellin-like effects on dwarf pea seedling growth. (LP) Nickell low-phosphate medium (*11*); (24) Burkholder and Nickell high-phosphate medium (*12*); (CM) coconut milk (18 percent by volume); (YE) Mead Johnson yeast extract (5 g/l); (2,4-D) 2,4-dichlorophenoxyacetic acid (0.6 part per million); (*p*Cl) *p*-chlorophenoxyacetic acid (0.6 part per million). Effects listed below are related to untreated plants (O) and gibberellin-treated (0.5 part per million) plants (++++).

Plant source	Common name	Plant part	Type tissue	Medium used	Relative effect
Vinca rosea	Periwinkle	Stem	Crown gall	LP	++
Helianthus annuus	Sunflower	Petiole	Crown gall	LP	+++
Melilotus officinalis	Sweet clover	Stem	Crown gall	LP-YE-*p*Cl	+
Melilotus officinalis	Sweet clover	Root	Virus tumor	24-YE-*p*Cl	+
Melilotus officinalis	Sweet clover	Stem	Virus tumor	24-YE-*p*Cl	+
Melilotus officinalis	Sweet clover	Root	Callus	LP	+
Agave toumeyana	Century plant	Leaf	Callus	White-2,4-D-CM	++
Ilex aquifolium	Holly	Stem	Callus	White-2,4-D-CM	+
Phaseolus vulgaris	Pinto bean	Cotyledon	Callus	White-2,4-D-CM	+

Some of the tissues whose extracts had a positive growth effect on the test plants are listed in Table 1. This represents about 50 percent of the plant tissues tested.

It should be noted that positive growth effects were obtained with extracts of both monocots and dicots, as well as with both leguminous and nonleguminous dicots. Activity is not limited by the type of tissue or by the plant part from which it originated, for stems, roots, leaves, and cotyledons are all represented, as well as nonpathological callus tissues and tissues of virus tumor and crown gall origin. This represents a wide distribution of plant material from many points of view: taxonomical, physiological, morphological, and pathological.

Responses of the magnitude obtained with the standard gibberellin solutions and with the plant extracts were not obtained with any other solutions of specific chemicals tested. These included several common auxins, purines, numerous antibiotics, organic acids, amino acids, and various types of chelating agents. Nor did the media on which the tissues were grown cause this response.

The production of substances which elicit a response in test plants similar to that elicited by the fungal metabolic products, the gibberellins, has been demonstrated for tissue cultures of higher plants—in many cases tissues which have been maintained for years on a synthetic medium. The wide variety of plants represented by these cultures lends strong support to the hypothesis that the

gibberellins, or at least gibberellin-like substances, are universal in the plant kingdom and might play a vital role in the control of plant growth (*10*).

Further work with those tissue cultures which produce the greatest amount of activity is being completed (*10*).

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New Maintenance Medium for Cell Culture

Although animal serum has been a necessary constituent of most media for continuous cell cultures (*1*), many sera contain "inhibitors" to a wide range of viruses (*2*). It would be desirable to replace serum with another substance which does not contain nonspecific inhibitors or antibody and which would sustain cells in a condition sensitive to viral effects during the necessary observation periods (*1*).

Having observed that boiled skim milk contributed to the maintenance of fully grown LAC cells (*3*), we undertook a study to determine the nutritive value of skim milk in cell culture maintenance media.

Skim milk was prepared by dissolving Pet instant nonfat dry milk in distilled water, according to instructions on the container, in order to reconstitute original volume. The milk was either boiled for 5 minutes or autoclaved at pressure of 7 lb. in.^{2} for 15 minutes. The *p*H was adjusted to 7.2 with sterile 5-percent sodium bicarbonate, and 150-ml aliquots were frozen at – 20°C. This material was designated as 100-percent skim milk.

Basal medium [medium 199 (*4*), or Eagle's basal medium (*5*), at *p*H 7.3 to 7.6] was mixed with varying amounts (0 to 100 percent final concentration) of skim milk and fed to LAC cells and HeLa cells (Gey). Maintenance was very satisfactory in the presence of skim milk (10 to 40 percent) in either basal medium. Final concentration of 20 percent of skim milk in medium 199 was selected for further experimental use. Cell strains monkey heart (Salk) and KB (Eagle) and rhesus monkey kidney cells were maintained in this medium for periods of up to 4 weeks when fed at 7-day intervals. Rhesus monkey kidney may also be maintained in Earle's balanced salt solution containing 20 percent skim milk and either 3 percent Travamin (*6*) or 0.5 percent lactalbumin hydrolyzate (*7*). A twofold concentrate of any one of these media may be mixed with agar for plaque overlay of rhesus monkey kidney cells. As with serum-containing maintenance medium, the degree of cell support by basal medium containing skim milk varies with different cell culture lines and different cell culture strains. Rounded cells and debris may accumulate, especially over the densest areas of cell cultures. Exceptionally dense areas of tube cultures may actually degenerate, leaving a wide margin of clear viable cells, which are suitable for observing viral effects.

The activity of skim milk appears to be associated with one or more of the milk proteins; the activity is not dialyzable and not sedimentable at 78,000g for 1 hour. A material of this type which retains its cell nutrient capacity after exposure to high temperature is rather unusual. Thus, skim milk is the first material which, at least partly, replaces the serum protein necessary for culture of HeLa cells, KB cells, and other continuous cell lines (*5*).

Skim milk medium is turbid, due to suspended casein (*8*), and it is rather striking to observe clearing of the milk medium under certain conditions. Trypsin, stool suspension, and some bacterial contaminations will clear the medium. Monkey kidney cell cultures also clear the medium after 3 to 5 days' incubation at 36°C, while HeLa, LAC, and KB cells do not, in the absence of serum. Proteolysis of the suspended casein is thought to be the mechanism of clearing.

The viral sensitivity of a cell culture in a maintenance medium is relative to its sensitivity in the presence of an established medium on the same cell culture line. In comparative titrations, 4- to 100-fold serum-inhibition of poliovirus was observed when calf-serum-containing maintenance medium was compared with serum-free medium on monkey kidney cells. A number of lots of heated skim milk were tested in this manner, at 20- and 30-percent concentration, without detection of decreased sensitivity. Similar determinations were made with monkey-kidney adapted Coxsackie B1, B2, B3, B4, B5, A7, A9 and vaccinia virus (*9*). There was no evidence that skim milk medium decreased cell culture sensitivity to these viruses. Preliminary studies indicate that HeLa cells in the presence of Ginsberg's medium are tenfold more sensitive to adenovirus 3 and 4 than HeLa cells in the presence of skim milk medium.

To determine whether the heating of skim milk would completely destroy any "antibodies" in milk (*10*), 1 ml of human serum containing antibodies to all three types of poliovirus was added to 9 ml of skim milk, and a 5-ml aliquot was autoclaved in the manner used to sterilize skim milk. The autoclaved aliquot was free of poliovirus inhibitors, demonstrating that the heating process completely destroyed the activity of the added poliovirus antibodies in skim milk. These results indicate that skim milk medium provides an environment which allows relatively full sensitivity to most of the viruses tested. Additional advantages are simplicity of preparation, low cost, and reduction in requisite frequency of feeding the cells.

Skim milk maintenance medium appears applicable as a standard medium for (i) comparative assay of a variety of viruses on a number of different cell cultures, (ii) safety testing of virus vaccines, (iii) isolation of viral agents which were not previously cultured, due to neutralization by serum-containing maintenance media, and (iv) detection of proteolytic activity of cell cultures.

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Blood Glucose of the Crab Hemigrapsus nudus

Studies in crustaceans of blood reducing substances, commonly referred to as "blood sugar," have been numerous. Until recently, however, there has been no means of establishing that the values obtained actually represent glucose, or indeed any other single substance. Attempts to increase specificity by use of fermentation methods (*1, 2*) still leave some question but indicate clearly that a substantial fraction of the reducing substances is not glucose. Recently Hu (*3*), using chromatographic methods, has shown that acid extracts of the shore crab *Hemigrapsus nudus* contain a variety of carbohydrates, some of which, at least, will probably also be present in the blood. It therefore appeared essential, as a basis for studies of carbohydrate metabolism in crustaceans, to learn whether glucose is actually present in normal blood and, if so, at what levels of concentration (*4*).

Crabs (*Hemigrapsus nudus*) were collected near Charleston, Oregon, and brought to the laboratory in Eugene, where they were maintained in seawater aquaria until blood was drawn, but no more than 5 to 10 days after capture. The stage of the animals in the intermolt cycle was determined by the method of Drach (*5*), as modified for this species by Kincaid and Scheer (*6*). Blood was drawn with a syringe through the coxal membrane of the fifth walking leg and was deproteinized by being heated for 15 to 30 seconds in a boiling water bath. Control experiments with other methods of deproteinization showed that this procedure gave reliable glucose values, and in view of the very low glucose concentrations found, it was considered desirable to avoid the dilution involved in other methods. Moreover, most other methods render the blood unsuitable for enzymatic procedures. Glucose was determined by the highly specific hexokinase-glucose-6-phosphate dehydrogenase (*Zwischenferment*) method (*7*), which depends on a spectrophotometric measurement of triphosphopyridine nucleotide reduction in the presence of adenosine triphosphate.

The mean blood glucose values, for the various intermolt cycle stages, for normal animals and for animals from which eyestalks had been removed 1 to 4 days before blood collection, are summarized in Table 1. From the values presented, it appears that the blood glucose of these crabs is very much lower than previous determination of blood reducing substances would indicate. No parallel measurements of reducing substances were made in these crabs, but determinations by means of the Folin-Wu method give values of about 15 mg/100 ml, and determinations of "total carbohydrate" with the anthrone method (*8*) give values of about 10 mg/100 ml. Evidently, then, less than 20 percent of the "blood sugar" is in fact glucose.

The variation with the intermolt cycle is also of interest. Renaud (*9*) found a gradual increase in blood reducing substances as the molt approaches in *Cancer pagurus*, as had other workers earlier. We had very few animals available in the premolt stages (D), but there is no sign of a premolt increase in blood glucose. Rather, the maximum values appear in stage C_1, in the early intermolt period; the mean for this stage is significantly higher than the means for stages B_2 or C_3, at a probability level of 0.5 percent on the basis of the *t* test.

Table 1. Mean values (in milligrams per 100 milliliters), and standard error of the means, for blood glucose of crabs (*Hemigrapsus nudus*) in relation to the intermolt cycle and to removal of eyestalks.

Item	Stage									
	Postmolt			Intermolt				Premolt		
	A_2	B_1	B_2	C_1	C_2	C_3	C_4	D_1	D_2	D_3
				Normal						
No.	6	4	10	7	6	12	8	3	1	2
Mean	1.55	1.23	1.12	2.55	1.85	1.28	1.70	2.45	0.75	2.11
Standard error	0.33	0.21	0.36	0.17	0.43	0.16	0.29			
				Eyestalkless						
No.			3	7	2	8	19		1	
Mean			0.56	1.87	5.03	1.20	1.22		1.21	
Standard error				0.35		0.25	0.23			

The values for eyestalkless animals in Table 1 are, in general, lower than the values for normal animals in the same stage of the cycle; however, the differences are not statistically significant. Scheer and Scheer (*2*) found a decrease in total and fermentable reducing substances in spiny lobsters and were able to explain the difference as resulting from an increased tissue utilization of glucose in eyestalkless aniamls. Kleinholz and Little (*1*) and Abramowitz *et al.* (*10*), however, could find no such decrease in crabs.

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Modes of Entry of Strontium into Plant Roots

Cell walls of roots consist of a framework of microfibrils (Fig. 1). Spaces between them may function as "free space" (*1*), or they may contain metabolic products, particularly pectic substances (*2*). Nutrient ions enter the root via free space or, as demonstrated below, by way of surface migration.

Cation-exchange membranes of the Amberplex type (*3*) were converted to H-membranes by leaching with normal HCl. Acid in the pore space of the membrane was removed by prolonged dialysis in distilled water.

To a wet Amberplex strip, 7.4 cm long, 1.5 cm wide, and 0.8 mm thick, was added 1.128 milliequivalents (meq) of $Sr(OH)_2$, tagged with Sr^{85}. This solution saturated the H-membrane to 80.0 percent. When it was immersed in 700 ml of distilled water, the strip released, at equilibrium, 0.084 μeq of strontium.

If an H-membrane of identical size is suspended in this solution (which is agitated and which contains the Sr-mem-

brane) the H-membrane will sorb dissolved strontium. Transfer of strontium from one membrane to the other via solution is very slow. Less than 0.05 percent of the strontium moves in 2000 hours. If the Sr-membrane is brought into intimate contact with the H-membrane, 42 percent of its strontium crosses the boundary within 48 hours.

Alfalfa seedlings, 16 days old, with a shoot length of 3 cm, were rinsed in distilled water for 4 hours. Forty-five plants, weighing 104 mg in an oven-dry state, were tied to the Sr-membrane strip in such a way that only the roots were in contact with it. The root-strip assembly was then immersed vertically in the equilibrium solution, which was aerated and stirred. Roots of an equal number of plants (102 mg), tied in a bundle, were also inserted into the solution. These roots never touhced the membrane. Strong artificial illumination was provided in all experiments.

After 18 hours both sets of plants were assayed for Sr^{85} (sets *A* in Table 1).

The uptake of Sr by contact was twice the uptake from the equilibrium solution, in spite of the fact that only a small portion of the root surface actually touched the membrane.

In set *B* there were 40 plants, 6 days old and weighing 69 mg, oven-dry. The membrane, as in *A*, was in a horizontal position, and the roots were pressed upon the strip with a 300-g weight. Between roots and weight was a layer of cotton. It seems fair to conclude that the higher activity of the *B* plants is due to more intimate contact of roots and strip caused by external pressure.

One cannot invoke the CO_2 theory as an alternate mechanism to contact-uptake, for the release of strontium from Amberplex during an 18-hour period is greater in distilled water freed from CO_2 than in water saturated with CO_2. If high concentrations of CO_2 near the root surface were crucial, the roots in contact with the membrane should sorb rather less strontium, not more, than the solution plants.

Related experiments were conducted with small beads of cation exchanger Chempro C-20 (*4*). This had an exchange capacity of 4.9 meq/g of oven-dry material. To 34.26 g of moist resin (19.1 percent H_2O) was added 122 meq of tagged $SrCO_3$ in 700 ml of solution. At equilibrium this solution contained 2.2 μeq of strontium, also in equilibrium with air.

The strontium-resin was scooped into a short vertical Lucite tube, the open bottom-end of which was covered with nylon gauze. The tube was lowered into the equilibrium solution in such a way that the upper level of the resin fill was horizontal with the level of the solution. The roots of 60 washed alfalfa seedlings, 10 days old and weighing 84 mg, were carefully packed into the resin slurry. Outside the tube, roots of an equal number of plants (98 mg) were inserted into the equilibrium solution, which was continually aerated.

After 18 hours the roots of the contact plants were rinsed in distilled water to free them from adhering resin beads. According to radioassay (Table 2), contact absorption again proved vastly superior to solution absorption. The plants in solution removed only 12 percent of the dissolved Sr.

One might contend that contact effects play no role whatever, that instead the roots excrete chelating substances which free the strontium from the resin particles, and that the strontium chelates then enter the root via free space.

To test this possibility, two strontium-resin columns, R-a and R-b, and two sand columns, S-a and S-b, were arranged in such a way that R-a was above S-a and R-b was above S-b. Alfalfa seedlings were inserted into the sand columns and into R-a but not into R-b. By means of a pumping arrangement, equilibrium solution was brought to the top of R-a. It percolated through the resin into sand column S-a and into a beaker, all by gravity. From the beaker the solution was pumped again on top of R-a, and percolation started anew. Circulation was continuous. The same process operated independently with R-b and S-b.

If the plants excrete chelating compounds, the resulting strontium chelates should, in considerable part, be leached from the resin into the sand. Plants in S-a should accumulate much more strontium than plants in S-b. But in duplicate experiments, each lasting 4 days, no significant differences between sand columns were found. The plants in resin accumulated 16.4 times more strontium than the plants in sand. Of course, if the resin should strongly adsorb the chelate, the chelate would not pass into the sand column, but neither would it diffuse into the free space of the root.

Although dissolved strontium can enter the root through free space, strontium adsorbed on resin cannot. We visualize a transfer of strontium from resin surface to root surface by contact exchange (*5*). Strontium may then migrate into the interior along negative surfaces of cell-wall constituents. We determined diffusion coefficients of strontium in Amberplex membrane ($D = 3 \cdot 10^{-8}$ cm^2/sec) and calculate that adsorbed strontium traverses a distance of 1 μ (corresponding to the thickness of cell walls) in about 1 minute. But ion-exchange migrations could not account for the appearance of substantial amounts of strontium in the leaves in 18 hours. Presumably, inside the root the adsorbed strontium is released into free space, or is acquired by carrier substances, or both, and is subsequently transported to the leaves.

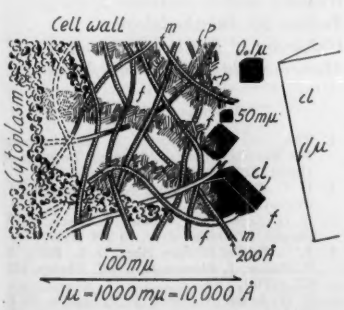

Fig. 1. Model of boundary region of root surface and growth medium. (*m*) cellulose microfibrils; (*p*) pectic substances; (*f*) free space; (*cl*) resin grains or clay particles of various sizes.

Table 1. Uptake of strontium by alfalfa seedlings (in microequivalents per gram of oven-dry material).

	Plants in solution A	Plants in contact with Amberplex	
		A	B
Leaves	0.005	0.023	0.071
Stems	0.086	0.053	0.105
Roots	0.298	0.641	1.043
Entire plant	0.059	0.104	0.174

Table 2. Uptake of strontium by alfalfa seedlings (in microequivalents per gram of oven-dry material).

	Plants in equilibrium solution	Plants in resin slurry
Leaves	0.0	3.6
Stems	4.2	15.5
Roots	16.9	107.1
Entire plant	2.8	17.8

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Acceleration of Plasma Cholinesterase Activity by Quaternary Ammonium Salts

It has been reported (*1*) that tryptamine (*2*) and some other alkylamines (*3*) accelerate the hydrolysis of benzoylcholine by plasma cholinesterase. In an attempt to obtain more information on the mechanism by which the enzyme activity is enhanced, we studied accelerating effect of relatively simple, closely related alkylamines. The compounds investigated were tetramethyl-, tetraethyl-, tetra-*n*-propyl, and tetra-*n*-butyl ammonium. For the sake of comparison, trimethyl- and triethylammonium and choline were also studied. Because of their poor solubility, the tripropyl and tributyl analogs could not be investigated.

The methods employed were similar to those used in work previously described (*4, 5*). The source of plasma cholinesterase was Cholase (*6*). Its activity was assayed with Kalow's (*7*) ultraviolet spectrophotometric and Warburg's manometric methods. The concentration of substrates at the start of the experiments was $5 \times 10^{-5}M$ in the spectrophotometric and $2 \times 10^{-3}M$ in the manometric experiments.

All tetraalkylammonium compounds accelerated the hydrolysis of benzoylcholine by plasma cholinesterase. The results of the spectrophotometric determinations are presented in Fig. 1. The activating effect increased from tetramethylammonium to tetra-*n*-propylammonium and then decreased sharply with the tetra-*n*-butyl compound. Similar results were obtained with benzoylcholine substrate in the manometric experiments. Qualitatively similar, but smaller (less than 100 percent), acceleration was observed with procaine substrate. Trimethyl- and triethylammonium also accelerated the hydrolysis of benzoylcholine, but to a lesser degree than the corresponding quaternary compounds. The increase in the rate of hydrolysis caused by $10^{-3}M$ concentrations of trimethyl-, tetramethyl-, triethyl- and tetraethylammonium were 10, 25, 105, and 160 percent, respectively. The activating effect of choline (32 percent), first reported by Hardegg *et al.* (*8*), was between that of tetramethylammonium and that of triethylammonium.

It is generally accepted that the active surface of the plasma cholinesterase contains an anionic and an esteratic site (*9*) and that various substrates containing both a positively charged N and a carbonyl group are attracted to the enzyme partly by coulombic forces operating between the opposite charged groups and partly by unspecific Van der Waals forces (*10*). It has also been shown that from the point of view of

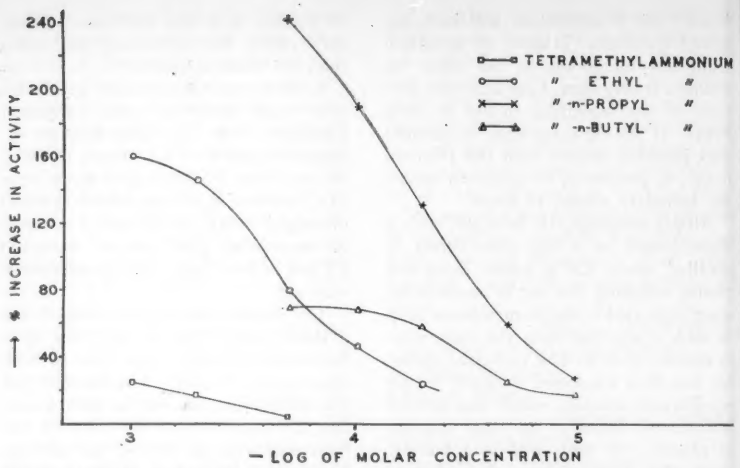

Fig. 1. Acceleration of the hydrolysis of benzoylcholine by quaternary ammonium salts.

functional activity, adsorption to the esteratic site is of greater importance than attraction to the anionic site (*4*). As was previously suggested (*2*), it is possible that the positively charged N of an aromatic substrate may get attached to the anionic site in a position which will prevent the attachment of the carbonyl C to the functionally important esteratic site. This would result in slowing of the rate of hydrolysis. If, on the other hand, the anionic site of the esterase is occupied by another positively charged group, the chances for the attachment of the ester group of the substrate to the esteratic site will increase, and the rate of hydrolysis will be accelerated.

The activating effect of the substituted ammonium compounds became greater when the length of the substituting alkyl radical increased from methyl to propyl. Substitution with progressively longer radicals increases the ionic radius and decreases the magnitude of the coulombic forces operating between the positively charged N and the anionic site of the enzyme. The fact that, despite this decrease in the magnitude of coulombic forces, the activating effect increased suggests that Van der Waals forces are also an important factor for the attachment of the activators to the anionic site of the enzyme.

On the basis of these considerations, the activating effect of tetra-*n*-butylammonium should be greater than that of the other quaternary ammonium salts investigated. In fact, however, the activating effect of tetra-*n*-butylammonium was less than that of either the tetraethyl or the tetra-*n*-propyl derivative. A possible explanation of this discrepancy might be that the radius of the tetra-*n*-butylammonium ion (> 6 A) is considerably greater than the assumed distance between the anionic and esteratic site of plasma cholinesterase (*4*). Consequently, when this ion becomes attached to the anionic site, because of its size, it may interfere with the access of the substrate to the esteratic site. This assumption is indirectly corroborated by the finding of Bergmann (*9*) that the inhibitory effect of tetra-*n*-butylammonium on the hydrolysis of acetylcholine substrate by plasma cholinesterase was greater than that of tetraalkylammonium salts of smaller molecular size.

The importance of ionic and other forces of attraction between the substrate and the cholinesterase molecule or between the inhibitor and the enzyme has been pointed out before by others (*11, 12*). This report discusses the role of these forces in the accelerating effect of alkylammonium derivatives on the hydrolysis of aromatic substrates by plasma cholinesterase.

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6. The compounds used in these studies were kindly supplied by the following individuals: Cholase, E. B. McLean, of Cutter Laboratories (Cholase is similar to plasma fraction IV-6-3; the plasma cholinesterase activity of

1 ml of Cholase corresponds to that of 160 ml of fresh, pooled, heparinized human plasma); benzoylcholine, L. A. Pirk of Hoffmann-LaRoche Inc.

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10 February 1958

Protection by D-Penicillamine against the Lethal Effects of Mercuric Chloride

The oral administration of the sulfhydryl amino acid, penicillamine, increases the urinary excretion of copper by normal individuals and by patients with hepatolenticular degeneration (*1*). Because of the afore-mentioned report and because of the interests of this laboratory in the metabolic and antimetabolic properties of penicillamine and its analogs (*2, 3*), the efficacy of this amino acid was compared with that of British antilewisite (BAL) as an antidote for heavy metal poisoning.

Male Sprague-Dawley rats (approximately 2½ months old, weight 280 to 340 g), housed in temperature- and humidity-controlled quarters (76°F, 50 percent) were used. As is demonstrated by the data of Table 1, while BAL (group II) completely protects rats against the lethal effects of a single intraperitoneal dose of 3.0 mg of mercuric chloride per kilogram, an equimolar amount of DL-penicillamine (group III) does not. When, however, an amount of D-penicillamine (group IV) equimolar to BAL, or a twice equimolar amount of DL-penicillamine (group V) is administered, a highly significant amount of protection is obtained. Since it appeared that the protective action of DL-penicillamine is due to the D-isomer (groups III, IV, and V), each of the enantiomorphs was tested. It was found that the protective action of penicillamine is primarily a property of the D-isomer (groups VII, VIII, and I). Whereas DL-cysteine (group VI) does not protect the animals, an equimolar amount of its β,β-dimethyl homolog, DL-penicillamine (group V), exerts a significant protective action.

The chronic oral use (*1, 4*) of DL-penicillamine in the treatment of various neurological disorders should be viewed with caution since weanling male Sprague-Dawley rats receiving two oral doses of 50 mg of DL-penicillamine per kilogram each day began to lose weight on the fifth day and four of ten animals were dead by the 13th day.

The biological activity of penicillamine has now been extensively studied (*2, 3, 5, 6*). Although for the rat (*5*) and *E. coli* (*3*) the L-isomer has growth inhibitory activity, the D-isomer is innocuous. While pyridoxine, ethanolamine, choline, or metabolites intermediate between the latter two compounds have been shown to reverse the growth-inhibiting activity of L-penicillamine in the rat (*5, 6*), only valine, isoleucine, leucine, or methionine will do so in *Escherichia coli* (*3*). These inhibitory properties of L-penicillamine and its relative ineffectiveness in treating heavy-metal poisoning appears to make D-penicillamine a safer and more effective agent than DL-penicillamine in the chronic treatment of hepatolenticular degeneration.

The oral effectiveness of D-penicillamine in stimulating copper excretion (*1*) and its intramuscular effectiveness in protecting rats against death due to mercuric chloride under the conditions of these experiments (*7*) presents the possibility of development of an oral prophylactic and an oral treatment for heavy-metal poisoning (*8*).

H. VASKEN APOSHIAN

Department of Pharmacology, Vanderbilt Medical School, Nashville, Tennessee

Table 1. Mortality of rats receiving mercuric chloride and sulfhydryl compounds. Statistical analysis of the groups showed $p > 0.05$ for groups I versus III, IV versus V, I versus VIII, and II versus VII; $p < 0.05$ for group VII versus group VIII; and $p < 0.01$ for groups I versus II, I versus IV, I versus V, I versus VII, III versus IV, III versus V, II versus IV. Pen, penicillamine; Cys, cysteine; BAL, British antilewisite.

Group	Compound (mg/kg)*	Cumulative 30-day mortality: No. dead/No. started, Expt. 1	Expt. 2	Expt. 3	Expt. 4	Expt. 5	Total	Survival (%)
I	3.0 $HgCl_2$	8/10	9/10	8/10	9/10	9/10	43/50	86
II	3.0 $HgCl_2$ + 60 BAL†	0/10	0/ 5	0/10			0/25	0
III	3.0 $HgCl_2$ + 72 DL-Pen†	6/10	9/10		7/10		22/30	73
IV	3.0 $HgCl_2$ + 72 D-Pen†		6/10	0/10	4/10		10/30	33
V	3.0 $HgCl_2$ + 144 DL-Pen‡		3/10	0/10	4/10		7/30	23
VI	3.0 $HgCl_2$ + 117 DL-Cys‡			9/10	10/10		19/20	95
VII	3.0 $HgCl_2$ + 144 D-Pen‡					5/20	5/20	25
VIII	3.0 $HgCl_2$ + 144 L-Pen‡					14/20	14/20	70
IX	144 DL-Pen‡		0/10				0/10	0
X	117 DL-Cys‡		0/10				0/10	0
XI	144 D-Pen‡		0/13				0/13	0

* All sulfhydryl compounds (*9*) were injected intramuscularly 20 minutes, 1½ hours, and 3½ hours after a single intraperitoneal injection of $HgCl_2$. Recorded amounts of the sulfhydryl compounds are of the free base and are the total of the three injections.
† Equimolar amounts. ‡ Equimolar amounts.

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7. This work was supported in part by a grant from the Surgeon General, Department of the Army. A preliminary report was presented at the September 1957 meeting of the American Society for Pharmacology and Experimental Therapeutics at Baltimore, Maryland. The technical assistance of Nancy S. Pointer is gratefully acknowledged.

8. Such experiments are in progress. Different dosage schedules, as well as modifications of the chemical structure of this compound, are being studied in an attempt to obtain 100-percent protection.
9. Sources of compounds: Redistilled BAL was the generous gift of Dr. J. H. Wells, Army Chemical Center, Md. Chromatographically pure DL-penicillamine, mp 204° to 205°C, was purchased from the Aldrich Chemical Company, D-Penicillamine HCl • ½H_2O $[\alpha]_D^{25} = -59.7$ (1 percent in 1*N* NaOH) and L-penicillamine HCl • ½H_2O $[\alpha]_D^{25} = +60.2$ (1 percent in 1*N* NaOH) were purchased from the California Foundation for Biochemical Research. Mallinckrodt's A. R. mercuric chloride was used. The solutions were such that 0.1 ml of a saline solution of mercuric chloride or sulfhydryl compound was injected per 100 g of body weight.

13 January 1958

Letters

Economics of Nuclear Power

The article by John E. Ullmann on "Economics of nuclear power" [*Science* **127**, 739 (1958)] reaches conclusions that appear to be based on highly tenuous assumptions. Basically, the findings of the author depend on a graphical extrapolation of past-performance trend lines. Such an evaluative technique, not coupled with a specific analysis of the processes involved, can readily produce misleading conclusions.

The assumption is made that the long-term pattern of cost reduction noted for conventional steam plants since 1910 to the present will prevail for nuclear power. However, inasmuch as the actual cost reduction in conventional plants has not been significant since 1945, it is further postulated that the trend will reverse and start to rise for the conventional steam plant. This up-for-one and down-for-the-other type of analysis completely ignores the common elements involved in the two processes being compared.

The author's study relates exclusively to steam power, inasmuch as he has specifically excluded from his analysis any direct-generation fission or fusion power which might circumvent the steam cycle. Thus, a proper steam-power analysis would require a distinction being made between those costs that are inherent to the use of a specific fuel and those costs that relate to the generation of steam irrespective of the nature of the fuel. If, as appears likely, those costs associated with steam generation per se will rise—and they represent a major aspect of the total cost of steam-power production—then such a rise will also be reflected in the projected nuclear power costs. This consideration would appear to invalidate a substantial portion of the author's analysis.

Further—and this was not even mentioned—actual fuel costs for nuclear versus conventional fuels are at present difficult to determine realistically. A substantial credit is now allowed for the used nuclear fuel, and this situation would presumably not prevail under competitive nonsubsidy conditions. Incidentally, reference 6 is in error and should refer to volume 77 (1955) [of *Trans. Am. Soc. Mech. Engrs.*].

HENRY KOLIN
Consolidation Coal Company, Library, Pennsylvania

In his article "Economics of nuclear power" [*Science* **127**, 739 (1958)], John E. Ullmann comes to some conclusions which are contrary both to economic analysis and to common sense. Ullmann predicts, for instance, that investment costs for conventional steam power plants will steadily increase in the future, whereas investment costs for nuclear power plants will decline continuously. Thus, he states that by 1966 investment costs per kilowatt of capacity will be equal, whereas by 1980 investment costs per kilowatt of capacity in conventional steam power plants will be close to $450 per kilowatt, while in nuclear power plants they will be around $50 per kilowatt.

As a nuclear power plant requires practically all the investments necessary in a conventional steam plant and, in addition, special investments for containment, control, safety, moderating and cooling materials, and so on, it is obvious that, per kilowatt of capacity, a nuclear power plant must, under existing and foreseeable technology, be more expensive than a conventional steam power plant. A calculation, therefore, which foresees higher investment requirements for a conventional power plant than for a nuclear power plant of the same size is as logical as a cost calculation which indicates that the construction of a whole house is cheaper than the construction of a single room in that house.

The United States Government in its

reply to the questionnaire of the Secretary-General of the United Nations assumed that, by 1975, investment costs for conventional power plants will amount to $150 per kilowatt and, for nuclear plants, to $300 per kilowatt, including fuel inventories [see *Economic Applications of Atomic Energy* (United Nations, New York, 1957), p. 83].

In addition to the point raised above, there are a number of other points in the article that might be challenged, in particular the method employed for forecasting power costs. This method, it is true, is frequently used by engineers, but its use is to be regretted as it has no sound economic basis. The highly speculative character of such forecasts should be made clear to the reader.

JOSEPH BARNEA
New York, New York

Both Kolin and Barnea seem to question my predictions for the same reason—my alleged failure to give weight to the common elements of conventional and nuclear power. These, however, are much less "common" than may at first appear. On the one hand, we have conventional equipment reaching a practical limit in size of units and a theoretical limit in operating conditions. On the other hand, in nuclear stations, steam operating conditions are now the same as in the conventional plants of 30 or 40 years ago, so that a cost reduction similar to that of the past seems to me to be very likely.

Nuclear plants can also be built much smaller, again paralleling conventional units for which the economic optimum size was much less in the past. The optimum size, in fact, went up with working temperature and pressure. The comparison of plants of "equal" size, as made by Barnea, is therefore not valid. In the words of his simile, the room is part of another house. Barnea's "extras" in nuclear plants have been declining in cost, as stated, and will no doubt continue to do so. In any case, their cost is offset by the elimination of much of the fuel- and ash-handling equipment in modern conventional plants. In part, they are included in the nuclear "boiler."

With regard to my statistical method, the confidence bands of extrapolations widen sharply as we go into the future. In this sense, all forecasts are speculative.

I agree with Kolin that nuclear fuel costs are quite artificial at present. Under freer conditions there is no reason why fuel reprocessing should not be done at a reasonable rate. Several large companies are interested in this field. The present distressed condition of the uranium mining industry also offers hope for cheap

nuclear fuel, especially if the dominant role of nuclear weapons in the market is eventually reduced.

Since my article was written several studies and proposals for plants in the United States and England have confirmed or even exceeded my expectations. Furthermore, as I am sure Barnea knows, we have just had a rate increase in New York, and more are to come. Kolin's "up-for-one and down-for-the-other" may well be upon us.

JOHN E. ULLMANN
Department of Industrial Engineering, Columbia University, New York

Meetings

Forthcoming Events

August

11–13. International Mathematical Union, 3rd general assembly, St. Andrews, Scotland. (F. Smithies, Mathematical Inst., 16 Chambers St., Edinburgh 1, Scotland.)

11–16. Occupational Therapists, World Federation's 2nd intern. cong., Copenhagen, Denmark. (Mrs. I. Worsoe, Hvidklovervej 10, Aarhus, Denmark.)

12–13. Economic Botany Conf., New York, N.Y. (D. J. Rogers, New York Botanical Garden, Bronx Park, New York 58.)

13–15. Electronic Standards and Measurements Conf., Boulder, Colo. (J. F. Brockman, National Bureau of Standards, Boulder.)

13–15. Industrial Applications of X-ray Analysis, 7th annual conf., Denver, Colo. (W. M. Mueller, Metallurgy Div., Denver Research Inst., University of Denver, Denver 10.)

13–19. Seaweed Symposium, 3rd Intern., Galway, Ireland. (C. O. hEocha, Chemistry, Department, University College, Galway.)

13–20. Insect Pathology and Biological Control, intern. conf., Prague and Smolenica, Czechoslovakia. (J. Weiser, Inst. of Biology, Nacvicisti 2, Prague XIX, Czechoslovakia.)

13–20. International Astronomical Union, 10th general assembly, Moscow, U.S.S.R. (P. Th. Oosterhoff, IAU, Leiden Observatory, Leiden, Netherlands.)

15–20. World Medical Assoc., 12th general, Copenhagen, Denmark. (World Medical Assoc., 10 Columbus Circle, New York 19.)

17. American College of Hospital Administrators, 24th annual, Chicago, Ill. (ACHA, 620 N. Michigan Ave., Chicago 11.)

17–21. Health Conf., 7th annual, University Park, Pa. (M. Cashman, Pennsylvania Dept. of Health, P.O. Box 90, Harrisburg.)

18–19. American Astronautical Soc., Western meeting, Palo Alto, Calif. (N. V. Petersen, Lockheed Missile Systems Div., Palo Alto.)

18–21. Conservation Education Assoc., 5th annual, Salt Lake City, Utah. (S. D. Mulaik, Biology Dept., University of Utah, Salt Lake City.)

18–21. Heat Transfer, AIChE conf., Evanston, Ill. (F. J. Van Antwerpen, AIChE, 25 W. 45 St., New York 36.)

18–22. Clinical Chemistry Workshop, Houston, Tex. (Division of Clinical Chemistry, Dept. of Biochemistry, Baylor Univ., College of Medicine, Houston 25.)

18–22. Occupational Medicine and Toxicology, 2nd Inter-American conf., Miami, Fla. (W. B. Deichmann, Dept. of Pharmacology, Univ. of Miami School of Medicine, Coral Gables, Fla.)

18–22. Plant Science Seminar, 35th annual, Big Rapids, Mich. (E. P. Claus, Div. of Pharmacy, Ferris Inst., Big Rapids.)

18–22. Semiconductors, intern. conf., IUPAP, Rochester, N.Y. (D. L. Dexter, Dept. of Physics, Univ. of Rochester, Rochester.)

18–23. New England Assoc. of Chemistry Teachers, 20th summer, Kingston, R.I. (J. A. Martus, College of the Holy Cross, Worcester 10, Mass.)

18–25. Religion in the Age of Science, 5th summer conf., Star Island, N.H. (Institute on Religion in an Age of Science, 280 Newton St., Brookline 46, Mass.)

20–23. Photofluorography, intern. cong., Stockholm, Sweden. (International Cong. of Photofluorography, P.O. Box 5097, Stockholm 5.)

(See issue of 20 June for comprehensive list)

Equipment

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■ COLORIMETER AND ABRIDGED SPECTROPHOTOMETER is based on the flicker-photometer principle. Illumination is provided by an incandescent source within an integrating sphere. Reflectance transmission measurements may be made on liquids or solids. Source filters permit comparison under standardized incandescent and daylight illumination. The instrument utilizes three solid-glass tristimulus filters and presents, on a meter, numerical values expressing difference between the sample and a reference standard. When it is used as an abridged spectrophotometer, the instrument divides the visible spectrum into ten bands. Visual inspection of the sample as seen by the instrument is also provided. Comparison sensitivity is 0.1 percent. (Instrument Development Laboratory, Inc., Dept. 169)

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National Bureau of Standards

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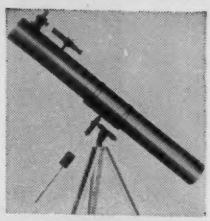

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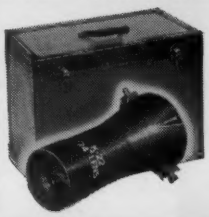

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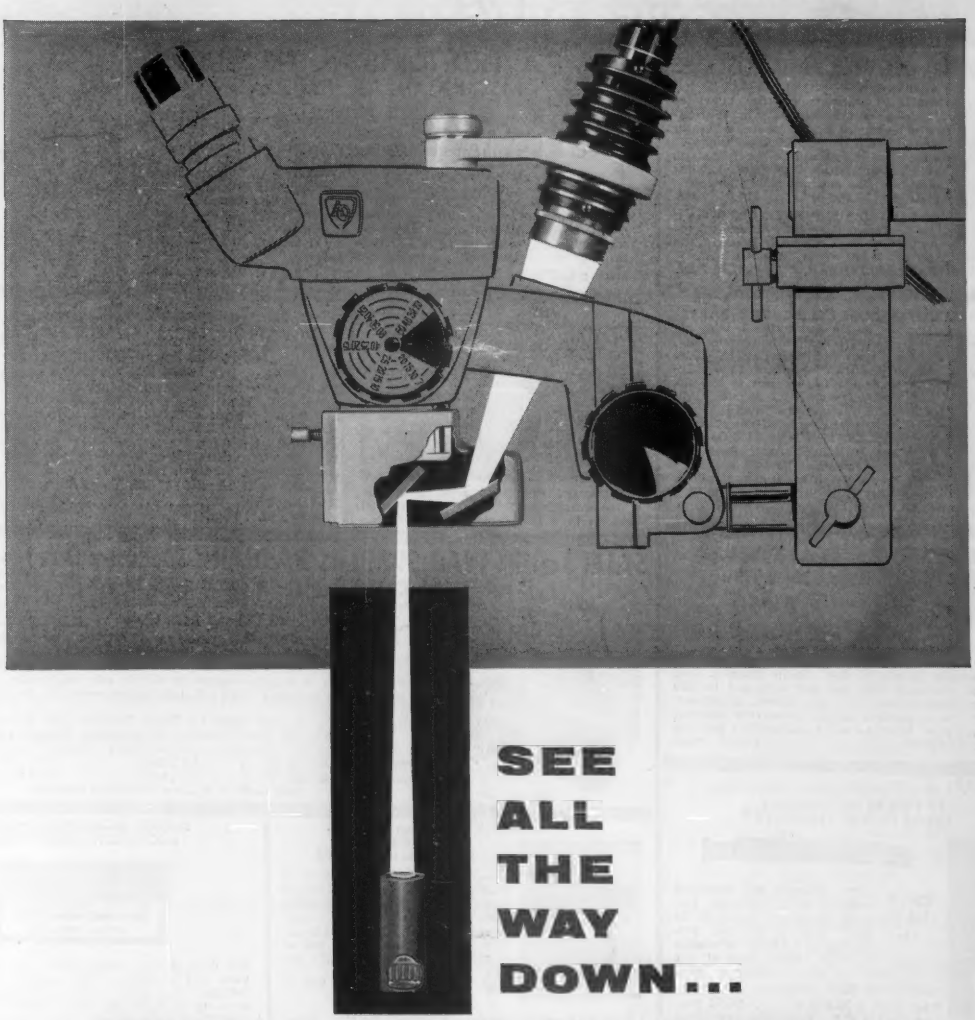

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